~~Confidential~~

Helsinki, 29 October 2021

Addressees
Registrant(s) of JS_Hexadecanedioic acid as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
18/01/2019

Registered substance subject to this decision ("the Substance")
Substance name: Hexadecanedioic acid
EC number: 208-013-5
CAS number: 505-54-4

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 ***8 May 2023***.

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

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

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

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

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

4. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: OECD TG 301B/C/D/F or OECD TG 310).

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

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487);

2. If negative results are obtained in 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).

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

1. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats;

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit);

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

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

Reasons for the 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". For references used in this decision, please consult the Appendix entitled "List of references".

Appeal

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

Failure to comply

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

Authorised[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

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

Appendix on Reasons common to several requests

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

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

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

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

Grouping of substances and read-across approach

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

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

i. Description of the grouping

In your registration dossier you have formed a group (category) of '*Dicarboxilic acids*'. You have provided a read-across justification document in IUCLID Section '*Linked Categories*', titled '[redacted]'.

For the purposes of this decision, the following abbreviations are used for the group members:

[1]	DC6	Hexanedioic acid, known as adipic acid (EC No. 204-673-3);
[2]	DC10	Decanedioic acid, known as sebacic acid (EC No. 203-845-5);
[3]	DC10Na	Disodium sebacate (EC No. 241-300-3);
[4]	DC11	Undecanedioic acid (EC No. 217-440-6);
[5]	DC12	Dodecanedioic acid (EC No. 211-746-3);
[6]	DC14	Tetradecanedioic acid (EC No. 212-476-9); and
[7]	DC16	Hexadecanedioic acid (EC No. 208-013-5), i.e. the Substance.

[2] Read-across assessment framework (RAAF, March 2017)
[3] RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)

You provide the following reasoning for the grouping the substances: "*Dicarboxilic acids are organic compounds that contain two carboxylic acid functional groups. They have the general type formula HOOC-(CH2)n-COOH.*".

You define the the structural basis for the grouping as "*dicarboxylic acids with straight carbon chain having a "n" value from 6 to 16"*.

ECHA understands that this is the applicability domain of the grouping and will assess your predictions on this basis.

B. Prediction of (eco)toxicological properties

***a.* Prediction of toxicological properties**

i. Mutagenity, Repeated Dose toxicity and Pre-natal Developmental toxicity

You have provided the following reasoning for the prediction of toxicity:: "*The physical and chemical properties as well as the toxicology and environmental fate and effects show that substances in this category have a similar order of toxicological and environmental fate properties".*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. ECHA understands that the properties of your Substance are predicted based on an identified trend within the group.

You intend to predict the properties for the Substance from information obtained from the following source substances:

In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.):
- DC10 (Shimizu H, 1985)
- DC12 ([redacted], 1999) with

In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.):
- DC6 (D Litton Bionetics, Inc., 1974)
- DC6 ([redacted] 1999)

Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.):
- DC10NA in rats (Greco, 1990)
- DC10NA in rabbits (Greco, 1990)

Pre-natal developmental toxicity study in a first species (Annex X, Section 8.7.2.):
- DC10NA (Greco, 1990)

ECHA notes the following shortcoming with regards to predictions of toxicity.

Data density

Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances.*

According to the ECHA Guidance, one of the factors in determining the robustness of a category is the density and distribution of the available data across the category.[4] To identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the category members needs to be available.

According to ECHA Guidance R.6, if toxicity is expected to vary in a regular pattern, the distribution of data across the category must cover the borders of the category in order to reliably establish the predicted trend. This is particularly important when the properties of a member situated at the border of a category are predicted.

Mutagenity

In your dossier, you have provided two *in vitro* gene mutation study in bacteria with DC10 and DC12, one *in vitro* chormossomal aberration study with DC6 and one *in vitro* micronucleous study with DC6.

In your justification document, you have provided a data matrix where you indicate that three category members (DC6, DC10, DC12) are not mutagenic.

Based on the information the data matrix, you conclude that "*They are neither mutagenic nor carcinogenic*.".

The information provided on *in vitro* gene mutation study in bacteria is obtained from the two category members (DC10 and DC12). The carbon chain length of these 2 category members locates these substances in the middle of the category's range of carbon chain length spanning from C6 to C16. Two data points in the middle of a category does not account for the range of structural variations across the category. Therefore, no reliable trend in the properties of the category members can be established as a result of the distribution of this information within the category.

Information on *in vitro* cytogenicity is only available from one member of the category, DC6. No trend in the variation of properties of a group of substances can be derived from a single data point.

Additionally, the Substance carries the longest carbon chain length of all the members of the category and is therefore located on the upper border of the category. In the absence of information on the Substance, the hypothesised trend in the variation of the properties of the category members within the given range of carbon chain length cannot be confirmed. Therefore, the information provided is not sufficient to establish that mutagenicity properties of the category members are likely to follow a regular pattern.

Repeated Dose Toxicity

In your dossier, you have provided two chronic studies with DC10Na, one in rat and one in rabbit.

In your justification document, you have provided a data matrix with results of repetead dose toxicity studies via oral route for three category members (DC6, DC10Na, DC12).

Based on these studies in the data matrix, you conclude that "*They do not produce systemic effects in repeated dose studies.*".

[4] ECHA Guidance R.6, Section R.6.2.1.5.

The study reports of the repeated dose toxicity studies with DC6 and DC12 mentioned in your justification document are not provided in the technical dossier. In the absence of this information, ECHA is not in a position to assess its reliability and, consequently, also its contribution to the demonstration of the hypothesised trend across the category.

Currently, information on repeated dose toxicity is only available in your dossier from one member of the category, DC10NA. No trend in the variation of properties of a group of substances can be derived from a single data point.

Furthermore, in the absence of information on the Substance, which is on the upper border of the category, the toxicity trend within the given range of carbon chain length cannot be confirmed. Therefore, the information provided is not sufficient to conclude that repeated dose toxicity properties of the category members are likely to follow a regular pattern.

Pre-natal Developmental Toxicity

In your dossier, you have provided one pre-natal developmental toxicity study with DC10Na, in rabbit.

In your justification document, you have provided a data matrix with results of pre-natal developmental toxicity studies for three category members (DC6, DC10Na, DC12).

Based on these studies in the data matrix, you conclude that the category members *"do not produce developmental/reproductive toxicity"*.

The study reports of the pre-natal developmental toxicity studies with DC6 and DC12 mentioned in your justification document are not provided in the technical dossier. In the absence of this information ECHA is not in a position to assess its reliability and, consequently, its contribution their to the demonstration of the hypothesised trend across the category. Currently, information on pre-natal developmental toxicity is only available from one member of the category, DC10NA. No trend in the variation of properties of a group of substances can be derived from a single data point.

Furthermore, in the absence of information on the Substance, which is on the upper border of the category, the toxicity trend within the given range of chain length cannot be confirmed. Therefore, the information provided is not sufficient to conclude that pre-natal developmental toxicity properties of the category members are likely to follow a regular pattern.

b. **Prediction for ecotoxicological properties**

i. Aquatic toxicity and Biodegradation

You have provided the following reasoning for the prediction of ecotoxicological and environmental fate properties: *"The physical and chemical properties as well as the toxicology and environmental fate and effects show that substances in this category have a similar order of toxicological and environmental fate properties"*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. ECHA understands that the properties of your Substance are predicted based on an identified trend within the group.

You intend to predict the properties for the Substance from information obtained from the following source substances:

Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- DC10 ([redacted] 1999)
- DC12 ([redacted] 2009)

Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- DC10 ([redacted] 2009)

Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- DC10 ([redacted]., 1999)
- DC12 ([redacted], 2009)

Ready biodegradability (Annex VII, Section 9.2.1.1.)
- DC12 ([redacted] 1989)

ECHA notes the following shortcoming with regards to predictions of ecotoxicity.

Data density

As stated under Prediction of toxicological properties above, reliable data density and distribution across the category, covering the borders of the category, is needed to identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category.

Aquatic toxicity

In your dossier, you have provided an algae growth inhibition study with DC10 and studies on short-term toxicity to fish and to aquatic invertebrates with DC10 and DC12.

In your justification document, you have provided a data matrix with results of aquatic toxicity studies for three category members (DC6, DC10, DC12):
- Data on algae growth inhibition, short-term toxicity to fish, short-term and long-term toxicity to aquatic invertebrates for DC6.
- Data on algae growth inhibition, short-term toxicity to fish and short-term toxicity to aquatic invertebrates for DC10 and DC12.

Based on these studies in the data matrix, you conclude that "*The environmental effects data are similar for most category members in that most members do not exhibit acute toxicity*.".

The study reports of the algae growth inhibition study with DC12 and of all the aquatic toxicity studies with DC6 mentioned in your justification document are not provided in the technical dossier. In the absence of this information ECHA is not in a position to assess its reliability and, consequently, its contribution their to the demonstration of the hypothesised trend across the category.

Currently, information on algae growth inhibition, short-term toxicity to fish and to aquatic invertebrates is obtained from the two category members (DC10 and DC12). The carbon chain length of these 2 category members locates these substances in the middle of the category's range of carbon chain length spanning from C6 to C16. Two data points in the middle of a category does not account for the range of structural variations across the category. Therefore, no reliable trend in the properties of the category members can be established as a result of the distribution of this information within the category.

Additionally, the Substance carries the longest carbon chain length of all the members of the category and is therefore located on the on the upper border of the category. In the absence of information on the Substance, the hypothesised trend in the variation of the properties of the category memberswithin the given range of chain length cannot be confirmed. Therefore, the information provided is not sufficient to conclude that aquatic toxicity properties of the cateogory members are likely to follow a regular pattern.

Biodegradation

In your dossier, you have provided a ready biodegradability study with DC12.

In your justification document, you have provided a data matrix where you indicate that three category members (DC6, DC10, DC12) are readily biodegradable.

Based on these studies in the data matrix, you conclude that all substances are readily biodegradable.

The study reports of the ready biodegradability study with DC6 and DC10 mentioned in your justification document are not provided in the technical dossier. In the absence of this information ECHA is not in a position to assess its reliability and, consequently, its contribution their to the demonstration of the hypothesised trend across the category.

Currently, information on ready biodegradability is only available from one member of the category, C12. No trend in the variation of properties of a group of substances can be derived from a single data point.

Additionally, as explained above, in the absence of information on the Substance (i.e. the upper border of the category), the hypothesised trend in the variation of the properties of the category members within the given range of chain length cannot be confirmed. Therefore, the information provided is not sufficient to conclude that ready biodegradability properties of the category members are likely to follow a regular pattern.

C. Conclusions on the grouping of substances and read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substances. 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.

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

2. Assessment of your weight of evidence adaptation under Annex XI, Section 1.2

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

- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

Your weight of evidence adaptation raises the same decifiencies irrespective of the information

requirement for which it is invoked. Accordingly, ECHA addressed these deficiencies in the present Appendix, before assessing the specific standard information requirements in the following appendices.

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

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

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

You have not included a justification for your weight of evidence adaptation, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation. Your weight of evidence approach has deficiencies that are common to all information requirements under consideration and also deficiencies that are specific for these information requirements individually. The common deficiencies are set out below, while the specific ones are set out under the information requirement concerned in the Appendices.

These issue(s) identified below are essential for all the information requirements in which you invoked a weight of evidence.

Reliability of the provided information with source substances

ECHA understands that you intend to predict the ecotoxicological properties of the Substance for the above listed endpoints, from data obtained with source substances in a read-across approach as part of your weight of evidence adaptation.

For the same reasons explained under Section 1 of the Appendix on Reasons common to several requests (i.e. Data density for Aquatic toxicity), the proposed read-across presents critical deficiencies.

Therefore, the information from the source substances submitted under your weight of evidence adaptation is not considered reliable.

Reliability of the provided information with QSAR estimations

ECHA understands that you intend to predict the ecotoxicological properties of the Substance for the above listed endpoints, by applying (a) (Q)SAR approach(es) in accordance with Annex XI, Section 1.3 as part of your weight of evidence adaptation.

Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

1. the prediction needs to be derived from a scientifically valid model,
2. the substance must fall within the applicability domain of the model,
3. results need to be adequate for the purpose of risk assessment or classification and labelling, and
4. adequate and reliable documentation of the method must be provided.

With regard to these conditions, we have identified the following issues:

The substance is outside the applicability domain of the model.

Under ECHA Guidance R.6.1.5.3., a substance must fall within the applicability domain specified by the model developer.

The applicability domain of the models you used is defined as neutral organic class, i.e. including "*non-reactive, non-ionizable organic compounds*".

The Substance has the following properties related to the estimation of applicability domain: it is a carboxylic acid.

The Substance is a carboxylic acid containing two ionisable groups and is not listed in the neutral organic class.

Therefore, you have not demonstrated that the Substance falls within the applicability domain of the model and the criteria specified in Annex XI, Section 1.3. are not fulfilled.

Based on the above, the information from QSAR estimations submitted under your weight of evidence adaptation is therefore not considered reliable.

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

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

1. In vitro gene mutation study in bacteria

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH (Grouping of substances and read-across approach), providing the justification examined in the Appendix on Reasons common to several requests, Section 1 above.

You have provided two key studies in your dossier:

i. *in vitro* gene mutation study in bacteria, (Shimizu H, 1985) with the source substance DC10;
ii. OECD 471, ([redacted] 1999) with the source substance DC12.

We have assessed this information and identified the following issues:

Your read-across adaptation is rejected for the reasons explained in the Appendix on Reasons common to several requests, Section 1.

On this basis, the information requirement is not fulfilled.

Study design

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

2. Short-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

You have adapted this information requirement under Section 1.5, Annex XI to REACH (Grouping of substances and read-across approach), providing the justification examined in the Appendix on Reasons common to several requests, Section 1 above.

You have provided the following information:

i. OECD TG 202, key study [redacted] 1999) with source substance DC10
ii. OECD TG 202 key study ([redacted], 2009) with source substance DC12

We have assessed this information and identified the following issues:

Whilst your read-across adaptation is rejected for the reasons explained in the Appendix on Reasons common to several requests, Section 1, ECHA has also identified the following endpoint specific issue with the adequacy and reliability of some of the source studies.

Under Annex XI, Section 1.5., the results to be read across must have an adequate coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

To fulfil the information requirement, a study must comply with OECD TG 202 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Technical specifications impacting the sensitivity/reliability of the test

- the test duration is 48 hours or longer;
- young daphnids, aged less than 24 hours at the start of the test, are used;
- the test concentrations are below the limit of solubility of the test material in the dilution water;

Characterisation of exposure

- the concentrations of the test material are measured at least at the highest and lowest test concentration, at the beginning and end of the test;
- the effect values can only be based on nominal or measured initial concentration if the concentration of the test material has been satisfactorily maintained within 20 % of the nominal or measured initial concentration throughout the test (see also ECHA Guidance R.7b, Section R.7.8.4.1);

Your registration dossier provides an OECD TG 202 with DC12 (study (ii)) showing the following:

Technical specifications impacting the sensitivity/reliability of the test

- the test duration was 24 hours;
- you have not specified if the test was conducted on neonates;
- the test concentration was 1000 mg/L and your report in your read-across justification document a limit of solubility of the test material in water of 40 mg/L

Characterisation of exposure

- no analytical monitoring of exposure was conducted;
- results are expressed based on nominal concentration.

Based on the above, there are major deficiencies impacting study (ii) with DC12, including the following:

Technical specifications impacting the sensitivity/reliability of the test and characterisation of exposure:

As you have performed a test with shorter duration and you have not indicated if the test was performed on neonates, it is not possible to conclude whether the absence of observed effect was due to lack of toxicity of the test material or a consequence of limited exposure time and/or lower sensitivity of the organisms due to developmental stage. Furthermore, you have used a test concentration above the water solubility of the test material. You report the results based on nominal concentration, but you have not perfomed analytical confirmation of exposure concentration. Therefore, you have provided no evidence that the exposure concentration was satisfactorly achieved and maintained during the test.

Therefore, the requirements of OECD TG 202 are not met.

As a consequence, study (ii) submitted in your adaptation does not provide a reliable coverage of the key parameters of the corresponding OECD TG and your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

The Substance is difficult to test due to the low water solubility (5.098 mg/L) and/or adsorptive properties (Log Kow of 4.67). OECD TG 202 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches,

if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

3. Growth inhibition study aquatic plants

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH (Grouping of substances and read-across approach), providing the justification examined in the Appendix on Reasons common to several requests, Section 1 above.

You have provided the following information:

i. key study, [redacted], 2009, according to ISO 10253 [*Water quality - Marine Algal Growth Inhibition Test with Skeletonema costatum and Phaeodactylum tricornutum*] () with source substance DC10

We have assessed this information and identified the following issue:

Whilst your read-across adaptation is rejected for the reasons explained in the Appendix on Reasons common to several requests, Section 1, ECHA has also identified the following endpoint specific issue with the adequacy and reliability of some of the source studies.

Under Annex XI, Section 1.5., the results to be read across must have an adequate coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

To fulfil the information requirement, a study must comply with OECD TG 201 (Article 13(3) of REACH) or with acceptable alternatives to OECD TG 201 (as listed in ECHA Guidance R.7b, Appendix R.7.8-2). Therefore, the following specifications must be met:

Characterisation of exposure

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (*i.e.* detection and quantification) and working range must be available. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;
- the results can be based on nominal or measured initial concentration only if the concentration of the test material has been maintained within 20 % of the nominal or measured initial concentration throughout the test;

Technical specifications impacting the sensitivity/reliability of the test

- the test concentrations are below the limit of solubility of the test material in the dilution water;

Reporting of the results

- the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;

Validity criteria
- exponential growth in the control cultures is observed over the entire duration of the test;
- at least 16-fold increase in biomass is observed in the control cultures by the end of the test;
- the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%;
- the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures is ≤ 7% in tests with *Pseudokirchneriella subcapitata* or *Desmodesmus subspicatus*. For other less frequently tested species, the value is ≤ 10%.

Your registration dossier provides one algae growth inhibition study with *Skeletonema costatum* according to an alternative to OECD TG 201 with DC10 showing the following:

Characterisation of exposure
- no analytical monitoring of exposure was conducted and no justification is provided whether analytical monitoring was not technically feasible;
- effect values are based on nominal concentrations and you claim that the '*substance was insoluble*';

Technical specifications impacting the sensitivity/reliability of the test
- the nominal test concentrations were from 3 to 320 mg/L. You do not report in your dossier a limit of solubility of the test material in the test medium (natural seawater), but you claim that the 'substance was insoluble';

Reporting of the results
- tabulated data on the algal biomass determined daily for each treatment group and control are not reported;

Validity criteria
- you have not specified if the validity criteria were met.

Based on the above, there are major deficiencies impacting the study, conducted according to an acceptable alternative to the OECD TG 201, including the following:
- *Characterization of exposure:* in the absence of analytical monitoring of effective exposure concentration or justification as to why analytical monitoring was not technically feasible, you have not demonstrated the stability of the test substance.
- *Technical specifications impacting the sensitivity/reliability of the test:* in the absence of information on solubility in pelagic test media, you have not demonstrated that the test concentrations were below the water solubility.
- *Reporting of results and validity criteria*: as you have not provided tabulated data on cell growth, it is not possible to verify that the validity criteria are met.

Therefore, the requirements of OECD TG 201 are not met.

As a consequence, the study submitted in your adaptation does not provide a reliable coverage of the key parameters of the corresponding OECD TG and your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

OECD TG 201 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 A.2.

4. Ready biodegradability

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

You have provided the following information:

i. an adaptation according to Annex XI, Section 1.5. (read-across), providing the justification examined in the Appendix on Reasons common to several requests, Section 1 above. You provided the following information:
   a. OECD TG 301 D key study ([redacted] 1999) with source substance DC12

ii. an adaptation according to Annex XI, Section 1.3. by providing the following information:
   a. QSAR prediction [EPISuite 4.1, BIOWIN model] key study (2017) for the Substance

We have assessed this information and identified the following issues:

i. Assessment of read-across adaptation

Your read-across adaptation is rejected for the reasons explained in the Appendix on Reasons common to several requests, Section 1.

ii. Assessment of QSAR adaptation

Annex XI, Section 1.3. specifies that the following conditions must be fulfilled whenever a (Q)SAR approach is used:

a) the prediction needs to be derived from a scientifically valid model,
b) the substance must fall within the applicability domain of the model,
c) results need to be adequate for the purpose of risk assessment or classification and labelling, and
d) adequate and reliable documentation of the method must be provided.

With regard to these conditions, we have identified the following issue:

Lack of or ina*dequate documentation of the prediction (QPRF)*

ECHA Guidance R.6.1.6.3 states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:

- the model prediction(s), including the endpoint,
- a precise identification of the substance modelled,
- the relationship between the modelled substance and the defined applicability domain,
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

You provided the following information about the prediction: ready biodegradability prediction of the Substance, using BIOWIN model with SMILES as input, claimed scientifically valid and relevant and performed according to ECHA guidance doument "How to use and report (Q)SARs

3.1". The information you provided about the prediction lacks the following elements: documentation of the prediction (QPRF).

In absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.
Therefore, your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

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

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

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH (Grouping of substances and read-across approach), providing the justification examined in the Appendix on Reasons common to several requests, Section 1 above.
You have provided the following information:

i. *In vitro* chromosome aberration study in mammalian cells (D Litton Bionetics, Inc., 1974) with the source substance DC6;
ii. *In vivo* mammalian bone marrow chromosome aberration test ([redacted] 1999) with the source substance DC6.

We have assessed this information and identified the following issues:

Whilst your read-across adaptation is rejected for the reasons explained in the Appendix on Reasons common to several requests, Section 1, ECHA has also identified the following endpoint specific issue with the adequacy and reliability of the source studies.

Study i.

Under Annex XI, Section 1.5., the results to be read across must have an adequate coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

The corresponding test method to fulfil this information requirement is the OECD TG 473. The key parameters of this test guideline include, amongst other: two separate test conditions must be assessed: in absence of metabolic activation and in presence of metabolic activation.

You registration dossier provides a study according to a test guideline equivalent to the OECD TG 473 on the source substance that investigates *in vitro* cytogenicity/chromosome aberration.

However, the robust study summary that you have provided for this study does not report that the key parameters of the OECD TG 473 listed above were investigated. The study was conducted in the absence of metabolic activation only.

Therefore, this study on the source substance DC6, as currently reported in your dossier, does not provide an adequate coverage of the key parameter(s) of the corresponding OECD TG and it cannot be used to predict the properties of the Substance.

Study ii.

Under Section 8.4.2., Column 2, first indent, Annex VIII to REACH, the study may be omitted "*if adequate data from an in vivo cytogenicity test are available*". ECHA Guidance[5] clarifies that the *in vivo* study must be either a micronucleus test or a chromosomal aberration test, performed according to OECD TG 474 or 475, respectively[6].

[5] ECHA Guidance R.7a, R.7.7.6.3, p.568
[6] ECHA Guidance R.7a, Table R.7.7–3, p.558

For the data from an *in vivo* cytogenicity test to be considered adequate, the *in vivo* study you submitted has to meet the requirements of the OECD TG 474 or OECD TG 475. The key parameters of the OECD TG 474 include, amongst other:

a) The study must include a minimum of three doses/groups of treated animals, as well as a negative control group and a positive control group.
b) Each group must have a minimum of 5 analysable animals (the test can be performed in either sex).
c) The proportion of immature among total (immature + mature) erythrocytes must be determined for each animal (by counting a total of at least 500 erythrocytes for bone marrow and 2000 erythrocytes for peripheral blood).
d) At least 4000 immature erythrocytes per animal must be scored for the incidence of micronucleated immature erythrocytes.
e) The proportion of immature erythrocytes among total erythrocytes and the mean number of micronucleated immature erythrocytes must be reported for each group of animals.

You registration dossier provides a study according to a test guideline equivalent to the OECD TG 474 on the source substance DC6 that investigates *in vivo* cytogenicity/chromosome aberration.

However, the robust study summary that you have provided for this study does not report that the key parameters of the OECD TG 474 listed above were investigated.

Therefore, this study on the source substance DC6, as currently reported in your dossier, does not provide an adequate coverage of the key parameter(s) of the corresponding OECD TG and it cannot be used to predict the properties of the Substance.

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.

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 appendices A.1. and B.1..

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

Your dossier does not contain any study or adaptation in accordance with column 2 of Annex VIII, Section 8.4.3. or with the general rules of Annex XI for this standard information requirement.

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.

Study design

To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

3. Screening for reproductive/developmental toxicity

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

Your dossier contains an adaptation justifying that an extended one-generation reproductive toxicity study does not need to be conducted because there are no results from available repeated dose toxicity studies that indicate adverse effects on reproductive organs or tissues.

The extended one-generation reproductive toxicity is not a standard information requirement at your tonnage level, as per Annex IX. Section 8.7.3, column 1. As indicated above, a screening for reproductive/developmental toxicity is an standard information requirement at your tonnage level.

According to Annex VIII, Section 8.7., Column 2, first paragraph, fourth indent, the study does not need to be conducted if a pre-natal developmental toxicity study (OECD TG 414) is already available.

In your dossier, you have provided information from a pre-natal developmental toxicity study conducted with the source substance DC10Na. However, your adaptation of the information requirement for a pre-natal developmental toxicity study is rejected for the reasons specified in appendix C.2.

Therefore, the information you provided does not fulfil the information requirement of Annex VIII, Section 8.7.1.

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[7] 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 under Section 1.5, Annex XI to REACH (Grouping of substances and read-across approach), providing the justification examined in the Appendix on Reasons common to several requests, Section 1 above.

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

You have provided the following information:

i. OECD TG 203 key study ([redacted] 2009) with source substance DC12
ii. OECD TG 203 key study ([redacted] 1999) with source substance DC10

We have assessed this information and identified the following issues:

Whilst your read-across adaptation is rejected for the reasons explained in the Appendix on Reasons common to several requests, Section 1, ECHA has also identified the following endpoint specific issue with the adequacy and reliability of some of the source studies.

Under Annex XI, Section 1.5., the results to be read across must have an adequate coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

To fulfil the information requirement, a study must comply with OECD TG 203 (Article 13(3) of REACH). Therefore, the following specifications must be met:

Technical specifications impacting the sensitivity/reliability of the test

- the test duration is 96 hours or longer;
- the test concentrations are below the limit of solubility of the test material in the dilution water;

Characterisation of the exposure:

- during the test, the concentrations of the test material are analysed at regular intervals;
- the results can be based on nominal or measured initial concentration only if there is evidence that the concentration of the test material has been maintained within 20 % of the nominal or measured initial concentration throughout the test;

Your registration dossier provides an OECD TG 203 with DC12 (study (i)) showing the following:

Technical specifications impacting the sensitivity/reliability of the test

- the test duration was 48 hours;
- the test concentration was 1000 mg/L and you report in your read-across justification document a limit of solubility of the test material in water of 40 mg/L;

Characterisation of exposure

- no analytical monitoring of exposure was conducted;
- results are expressed based on nominal concentration.

Based on the above, there are major deficiencies impacting study (i) with source substance DC12, including the following:

- *Technical specifications impacting the sensitivity/reliability of the test and characterisation of exposure*: as you have performed a test with shorter duration it is not possible to conclude whether the absence of observed effect was due to lack of toxicity of the test material or a consequence of limited exposure time. Furthermore, you have used a test concentration above the water solubility of the test material. You report the results based on nominal concentration, but you have not performed analytical confirmation of exposure concentration. Therefore, you have provided no evidence that the exposure concentration was satisfactorily achieved and maintained during the test.

Therefore, the requirements of OECD TG 203 are not met.

As a consequence, the study (i) submitted in your adaptation does not provide a reliable coverage of the key parameters of the corresponding OECD TG and your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

OECD TG 203 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 A.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) in rodents is a standard information requirement in Annex IX to REACH.

You have adapted this information requirement under Section 1.5, Annex XI to REACH (Grouping of substances and read-across approach), providing the justification examined in the Appendix on Reasons common to several requests, Section 1 above.

You have provided the following information:

i. Chronic toxicity: oral feed study in rat (Greco, 1990) with the source substance DC10Na (key study);
ii. Chronic toxicity: oral feed study in rabit (Greco, 1990) with the source substance DC10Na (supporting study).

We have assessed this information and identified the following issues:

Whilst your read-across adaptation is rejected for the reasons explained in the Appendix on Reasons common to several requests, Section 1, ECHA has also identified the following endpoint specific issue with the adequacy and reliability of some of the source studies.

Under Annex XI, Section 1.5., the results to be read across must have an adequate coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

Study i.:

The corresponding test method to fulfil this information requirement is the OECD TG 408. The key parameters of this test guideline include, amongst other: clinical observations, ophthalmological examination, sensory reactivity to various stimuli and functional observations of the animals, recording of body weight, a set of hematology and clinical biochemistry measurements, and full detailed gross necropsy and subsequent macroscopic examinations and histopathology of a set of organs and tissues.

Your registration dossier provides a chronic study (study i.) in rats that investigates the toxicity of the source substance DC10Na after daily administration of the substance to rats via their diet over a period of 6 months.

However, the robust study summary that you have provided for this study does not report that the key parameters of the OECD TG 408 listed above were investigated in this study on the source substance DC10Na.

Therefore, this study on the source substance DC10Na does not provide an adequate coverage of the key parameter(s) of the corresponding OECD TG and it cannot be used to predict the properties of the Substance.

Study ii.:

Under Annex XI, Section 1.5., the results to be read across must have an adequate coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

Annex IX, 8.6.2, column requires that information from a sub-chronic toxicity study performed in a rodent species be provided. The corresponding test method to fulfil this information

requirement is the OECD TG 408. The key parameters of this test guideline include, amongst other that the study is conducted in a rodent species.

Your registration dossier provides a chronic study (study ii.) that investigates the toxicity of the source substance DC10Na after daily administration of the substance to rabbits via their diet over a period of 6 months.

The source study ii. provides information on a non-rodent species, the rabbit.
Therefore, the study ii. does not provide relevant information in rodents as required by the Annex IX, Section 8.6.2, column 1 and it cannot be used as source study to predict the properties of the Substance.

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 because the Substance is reported to occur as a dust without a significant proportion (>1% on weight basis) of particles of inhalable size (MMAD < 50 µm).

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

2. Pre-natal developmental toxicity study in one species

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH (Grouping of substances and read-across approach), providing the justification examined in the Appendix on Reasons common to several requests, Section 1 above.

You have provided the following information, a pre-natal developmental toxicity study in rabbit (Greco, 1990) with DC10Na (key study);

We have assessed this information and identified the following issues:

Whilst your read-across adaptation is rejected for the reasons explained in the Appendix on Reasons common to several requests, Section 1, ECHA has also identified the following endpoint specific issue with the adequacy and reliability of some of the source studies.

Under Annex XI, Section 1.5., the results to be read across must have an adequate coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

The corresponding test method to fulfil this information requirement is the OECD TG 414.
The following key parameter(s) of this test guideline include, among others:

a) 20 female animals with implantation sites for each test and control group;
b) examination of the dams for weight and histopathology of the thyroid gland, gravid uterus weight, uterine content, body weight of the dams, clinical signs of the dams (e.g.food consumption);
c) examination of the foetuses for sex and body weight. external, skeletal and soft tissue alterations (variations and malformations) and number of resorptions and or live foetuses.

Your registration dossier provides a developmental toxicity study in rabbit on the source

substance DC10Na. Based on the information provided in your dossier, the source substance was administered to 20 pregnant rabbits for a period of 25 days. After 25 days, 10 animals were sacrificed and "*fetuses and reproduction organs of all animals (uterus, placenta, ovaries) were weighed post mortem and examined macroscopically as well as histologically*". The remaining 10 animals and their offspring were dosed for another 3 months before sacrifice.

However, the robust study summary that you have provided for this study does not report that the key parameters of the OECD TG 414 listed above were investigated.

Therefore, this study on the source substance DC10Na does not provide an adequate coverage of the key parameter(s) of the corresponding OECD TG and it cannot be used to predict the properties of the Substance.

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[8] administration of the Substance.

3. Long-term toxicity testing on aquatic invertebrates

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

You have provided the following information:

i. 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: "*According to Column 2 of Annex IX of REACH Regulation 1907/2006, long-term toxicity testing on daphnie shall not be conducted since the chemical safety assessment does not indicate a risk for aquatic organisms.";*

ii. an adaptation according to Annex XI, Section 1.2. of REACH (weight of evidence). In support of your adaptation, you provided the following set of information:
   a. ECOSAR prediction from 2019, claimed to follow ECHA guidance R.6
   b. A justification to use the source data on short-term aquatic invertebrates toxicity mentioned in Appendix A.2, including:
      i. OECD TG 202 key study ([redacted] 1999) with source substance DC10
      ii. OECD TG 202 key study ([redacted] 2009) with source substance DC12

You conclude that based on this information: "*hexadecanedioic acid is not expected to be toxic for the aquatic species on the long term. Hexadecanedioic acid is therefore not classified for aquatic chronic toxicity*".

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

i. Adaptation based on Annex IX, Section 9.1, Column 2

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.

ii. Adaptation based on Annex XI, Section 1.2

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

As explained under Appendix on Reasons common to several requests, Section 2, the weight of evidence must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.5 at Annex IX includes similar information that is produced by the OECD TG 211. This includes:

1) the time to production of the first brood and reproductive output of *Daphnia* sp. expressed as the total number of living offspring produced at the end of the test, and
2) the survival of the parent animals during the test.

1. *Concerning key parameters (1) time to produce the first brood and reproductive output of Daphnia*

The source of information (a) may provide relevant information on this key parameter. However, the reliability of this source of information is significantly affected by the deficiency identified and explained under Appendix on Reasons common to several requests, Section 2, above (Reliability of the provided information with QSAR estimations).

2. *Concerning key parameter (2) survival of parental animals*

The sources of information (a), (b.i) and (b.ii) may provide relevant information on this key parameter.

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

(a) Reliability of the QSAR information

The reliability of source of information(s) is significantly affected by the deficiency identified and explained under Appendix on Reasons common to several requests, Section 2, above.

(b) Reliability of short-term toxicity data

The reliability of sources of information (b.i) and (b.ii) is significantly affected by the deficiencies identified and explained under Appendix on Reasons common to several requests, Section 1 (i.e. Data density for Aquatic toxicity).

The conditions of exposure in OECD TG 211 specifies that the test duration is 21 days or sufficient to produce at least three broods.

Both sources of information (b.i) and (b.ii) have shorter duration (i.e. 48 hours and 24 hours, respectively) than foreseen in a long-term toxicity study. This condition of exposure is essential because the effects observed in a long-term study might be considerably more pronounced than over a shorter study duration. Therefore, the provided studies cannot be considered reliable sources of information that could contribute to the conclusion on this key parameter investigated by the required study.

Conclusion

Taken together, sources of information as indicated above, provide information on survival of

parental animals but information on reproductive output and production of first offspring is not provided. Furthermore, the information provided on survival of parental animal is not reliable. Therefore, your proposed conclusion that the substance is not hazardous and should not be classified for aquatic chronic toxicity is unsupported.
Accordingly, 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 forseen to be investigated in an OECD TG 211 study.
Therefore, your adaptation is rejected and the information requirement is not fulfilled.

Study design

OECD TG 211 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 A.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:

i. 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: "Ac*cording to Column 2 of Annex IX of REACH Regulation 1907/2006, long-term toxicity testing on fish shall not be conducted since the chemical safety assessment does not indicate a risk for aquatic organisms.";*

ii. an adaptation according to Annex XI, Section 1.2. of REACH (weight of evidence). In support of your adaptation, you provided the following set of information:
   a. ECOSAR prediction from 2019, claimed to follow ECHA guidance R.6
   b. A justification to use the source data on short-term fish toxicity already, mentioned in Appendix B.4, including:
      i. OECD TG 203 key study ([redacted], 2009) with source substance DC12
      ii. OECD TG 203 key study ([redacted] 1999) with source substance DC10

You conclude that based on this information: "*hexadecanedioic acid is not expected to have long term effects on fish. Hexadecanedioic acid is not expected to be classified for aquatic chronic toxicity*".

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

i. Adaptation based on Annex IX, Section 9.1, Column 2

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.

ii. Adaptation based on Annex XI, Section 1.2

As explained under Appendix on Reasons common to several requests, Section 2, the weight of evidence must fulfil the information requirement based on relevant and reliable sources of

information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.6 at Annex IX includes similar information that is produced by the OECD TG 210. This includes:

1. stage of embryonic development at the start of the test, and
2. hatching of fertilized eggs and survival of embryos, larvae and juvenile fish, and
3. appearance and behaviour of larvae and juvenile fish, and
4. weight and length of fish at the end of the test.

1. *Concerning key parameters (1) stage of embryonic development at the start of the test and (4) weight and length of fish at the end of the test*

   None of the sources of information investigate these key parameters. Therefore, they do not provide information that would contribute to the conclusion on these key parameters.

2. *Concerning key parameter (2) hatching of fertilized eggs and survival of embryos, larvae and juvenile fish*

   The sources of information (a), (b.i) and (b.ii) may provide partially relevant information on this key parameter since they may provide information on survival of juvenile fish.

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

(a) Reliability of the QSAR information

The reliability of source of information(s) is significantly affected by the deficiency identified and explained under Appendix on Reasons common to several requests, Section 2, above (Reliability of the provided information with QSAR estimations).

(b) Reliability of short-term toxicity data

The reliability of sources of information (b.i) and (b.ii) is significantly affected by the deficiencies identified and explained under Appendix on Reasons common to several requests, Section 1 (i.e. Data density for Aquatic toxicity).

The conditions of exposure in OECD TG 210 specifies that the test should start as soon as possible after the eggs have been fertilised until species-specific time period that is necessary for the control fish to reach a juvenile life-stage (28 to 60 days post-hatch).

Both sources of information (b.i) and (b.ii) have shorter duration (i.e. 48 hours and 96 hours, respectively) than foreseen in a log-term toxicity study. This condition of exposure is essential because the effects observed in a long-term study might be considerably more pronounced than over a shorter study duration. Therefore the provided studies cannot be considered reliable sources of information that could contribute to the conclusion on this key parameter investigated by the required study.

3. *Concerning key parameter (3) appearance and behaviour of larvae and juvenile fish*

The source of information (a) does not investigate these key parameters and (b.i) does not provide this information however (b.ii) provides partially relevant information since it provides information on abnormal behaviour of fish.

However, as explained under point (2)(b) above, the reliability of source of information (b.ii) is significantly affected.

Conclusion

Taken together, sources of information as indicated above provide information on long-term toxicity to fish (survival and behaviour of juvenile fish) but essential parts of information of the dangerous property is lacking. Furthermore, the information provided on these key investigations is not reliable. Therefore, your proposed conclusion that the substance is not hazardous and should not be classified for aquatic chronic toxicity is unsupported.

Accordingly, 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 forseen to be investigated in an OECD TG 210 study.
Therefore, your adaptation is rejected and the information requirement is not fulfilled.

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.).

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 A.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[9].

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[10].

9

10 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 07 December 2020.

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

ECHA did not receive any comments within the commenting period.

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[11] 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)[12]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[13]

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[14]

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

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.