~~Confidential~~

Helsinki, 10 November 2021

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

Date of submission of the dossier subject to this decision
13/08/2014

Registered substance subject to this decision ("the Substance")
Substance name: Isoamyl xanthate
EC number: 807-374-1
CAS number: 2540-36-5

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 ***17 August 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. Surface tension (Annex VII, Section 7.6.; test method: EU A.5./OECD TG 115)

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

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

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

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

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

2. If negative results are obtained in tests performed for the information requirement of Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

3. Short-term repeated dose toxicity (28 days; Annex VIII, Section 8.6.1.) to be combined with the Screening for reproductive/developmental toxicity below

4. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test

method: EU B.64/OECD TG 422) by oral route, in rats

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

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 VIII of REACH", respectively.

Information required depends on your tonnage band

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

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

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 gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- 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.)

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[2] and related documents[3, 4].

A. Predictions for (eco)toxicological properties

You have provided a read-across justification in the CSR.

You read-across between the analogue substances:

1) Dithioxomethane / carbon disulphide (EC 200-843-6)
2) 3-Methyl-butan-1-ol (EC 204-633-5),
3) Pentan-1-ol (EC 200-752-1)
4) Potassium O-butyl dithiocarbonate (EC 212-808-2)
5) Potassium O-ethyl dithiocarbonate (CAS 140-89-6; EC 205-439-3)
6) Potassium O-isobutyl dithiocarbonate (CAS 13001-46-2; EC 235-837-2)
7) Potassium O-pentyl dithiocarbonate (CAS 2720-73-2; EC 220-329-5)
8) Sodium O-ethyl dithiocarbonate (CAS 140-90-9; EC 205-440-9)

[2] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals. 2008 (May) ECHA, Helsinki. 134. pp. Available online: https://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf/77f49f81-b76d-40ab-8513-4f3a533b6ac9

[3] 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)

[4] 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

9) Sodium O-isobutyl dithiocarbonate (CAS 25306-75-6; EC 246-805-2)
10) Sodium O-isopropyl dithiocarbonate (CAS 140-93-2; EC 205-443-5
11) Dithiocarbonic acid O-ethyl ester (CAS 151-01-9; EC 205-780-8)
12) O-isopropyl hydrogen dithiocarbonate (CAS 140-92-1; EC 205-441-4)

as source substances and the Substance as target substance.

You have provided the following reasoning for the prediction of (eco)toxicological properties: and "*This substance is hydrolytically unstable. As it is used in water solutions the systemic adverse effects are related to the main degradation products. It will decompose in water releasing mainly carbon disulphide and particular alcohols (3-methyl-butan-1-ol and pentan-1-ol). The decomposition rate is dependent on the pH, temperature and the concentration of the substance in water solutions.* […] *Since CS2 is the most volatile and the most hazardous degradation product, it is the driving force for the hazard assessment of the target substance."* and *"xanthates can be considered as a group of substances which have structural similarity and similar behaviour in contact with water and in the physiological processes, their irritation as well as acute and systemic adverse effects to human health are similar. Therefore, […] the read-across data from the analogue xanthates is used to evaluate the irritation, and short term and/or long-term toxicological effects of the target substance"*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which

(1) is based on the formation of common (bio)transformation products. The properties of your Substance are predicted based on a based on a worst-case approach.

Based on the studies you provided with the source substances 4)-11), ECHA understands that you predict the properties of the Substance also using a read-across hypothesis which

(2) assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

ECHA notes the following shortcoming(s) with regards to prediction(s) of toxicological and ecotoxicological properties.

1. Supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[5]. 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 analogue substances.

Supporting information must include information on the rate of formation of the common compounds (e.g. toxicokinetic studies) and, for the prediction based on similar effects by different substances, bridging studies to compare properties between the Substance and the analogue substances.

a. Missing information on the formation of common compound

As indicated above, your read-across hypothesis (1) is based on the (bio)transformation of

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

the Substance and of the source substance(s) to a common compound(s). In this context, information characterising the rate and extent of the transformation of the Substance and of the source substance(s) is necessary to confirm the formation of the proposed common transformation product and to assess the impact of the exposure to the parent compounds.

You have not provided any experimental data or other adequate and reliable information, neither about the transformation (hydrolysis) nor any other toxicokinetic behaviour of your Substance.

In the absence of this information, you have not provided supporting evidence establishing that the proposed common transformation product is formed as assumed in your read-across hypothesis. Therefore, you have not provided sufficient supporting information to strengthen the rationale (1) for the read-across.

b. Missing information to compare properties of the analogue substances

As indicated above, one of your read-across hypothesis (2) is based on the assumption that the structurally similar analogue substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Subtance and the analogue substances is necessary to confirm that the substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the substances.

While you have included information on the source substances in your dossier, there is no information available with the Substance. The data set reported in the technical dossier does not include relevant, reliable and adequate information for the analogue substances to support your read-across hypothesis.

In the absence of such information, you have not established that the source substances and the Substance are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale (2) for the read-across.

2. Bias in the choice of source studies/substances

In order to make an accurate prediction of (eco)toxicological properties, all relevant information must be considered in the prediction. If not all information is considered in the read-across approach, then there is a risk of bias to be introduced in predictions. Bias may be caused by incorrect/incomplete selection of source substance(s); or due to a particular selection of source study(ies). If all information on all the substances in the category has not been considered, then this may result in an over/under estimation in the prediction[6].

Positive results are observed in the publicly available *in vitro* gene mutation study in mammalian cells conducted with the analogue substance potassium isopentyl dithiocarbonate (EC 213-180-2), while a QSAR prediction is provided in your dossier for in vitro gene mutation study in mammalian cells information requirement with negative outcome. The analogue substance potassium isopentyl dithiocarbonate is also a xanthate substance, but no scientific reason was provided for considering only other xanthate substances in your read-across justification for all (eco)toxicological endpoints.

[6] 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)Section 4.5.1.5.

There are data available that give rise to a greater concern than the source studies you use as key studies, but that you have not considered Therefore, your predictions are biased and may underestimate the hazard of the substance.

3. Adequacy and reliability of source study

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

i. be adequate for the purpose of classification and labelling and/or risk assessment;
ii. have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);
iii. cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.
iv. adequate and reliable documentation of the applied method, including robust study summary(ies) of the source study(ies) must be provided.[7]

Your dossier does not contain any robust study summaries for the source substances 1), 2) and 3) listed under **A.** above for the endpoints repeated dose toxicity and toxicity to reproduction.

In the absence of robust study summaries for all relevant source substances under each endpoint for which a read-across adaptation is attempted, criterion iv) is not met and it is not possible to independently assess whether the criteria i), ii) and iii) above are met.

B. Conclusions on the read-across approach

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

In your comments to the draft decision you indicate your agreement to the draft decision and state that "*the endpoints addressed in the Draft Decision will need further improvement to bring up to expected standards*".

More specifically, you state that "*some additional 'anchor' studies are needed across the range to establish a valid group, including proposals for work to demonstrate shared degradation pathways to alcohol and carbon disulphide*", and indicated your intention to prepare a read-across category for the Substance and the analogue substances

EC 205-440-9 Sodium ethyl xanthate
EC 205-439-3 Potassium ethyl xanthate
EC205-443-5 Sodium isopropyl xanthate
EC205-441-4 Potassium isopropyl xanthate
EC 235-837-2 Potassium isobutyl xanthate
EC 213-180-2 Potassium isoamyl xanthate

In your comments you did not provide further details or supporting documentation for the category being prepared.

[7] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.6.1

On this basis, the information in your comments is not sufficient for ECHA to make an assessment. Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "*How to act in Dossier Evaluation)*."

2. Assessment of your QSAR adaptation under Annex XI, Section 1.3.

You seek to adapt the following standard information requirements by using data from Qualitative or quantitative structure-activity relationship (QSAR) in accordance with Annex XI, Section 1.3:

- *in vitro* gene mutation study in bacteria
- *in vitro cytogenicity study in mammalian cells or in vitro micronucleus study*
- *in vitro* gene mutations in mammalian cells
- sub-acute toxicity study (28-day)
- screening study for reproductive/developmental toxicity

ECHA assessed this information and identified the following issue:

Annex XI, Section 1.3. states that results obtained from valid QSAR models may be used instead of testing when the following cumulative conditions are met, in particular:

1. results are derived from a QSAR model whose scientific validity has been established;
2. the substance falls within the applicability domain of the QSAR model;
3. adequate and reliable documentation of the applied method is provided; and
4. the results are adequate for classification and labelling and/or risk assessment.

A QSAR Model Reporting Format (QMRF) and a QSAR Prediction Reporting Format (QPRF) are required to establish the scientific validity of the model, to verify that the Substance falls within the applicability domain of the model, and to assess the adequacy of the prediction for the purposes of classification and labelling.[8]

Shortcomings in the prediction of toxicological properties

You have provided QSAR predictions for the endpoints listed above in order to comply with the REACH information requirements.

A. You have not provided sufficient documentation for the QSAR predictions for the following endpoint and study:

- In vitro mutations in bacteria (study iii), predictions for sodium ethyl xanthate (EC 205-440-9), sodium isopropyl xanthate (EC 205-443-5) and sodium isobutyl xanthate (EC 246-805-2)) (

In particular you have not included QMRFs and/or a QPRFs in your technical dossier for the study listed above.

You have not provided information to demonstrate the scientific validity of the QSAR models (including details on the predicted endpoints), and that the Substance falls within their applicability domains.

[8] For further information, see ECHA Guidance R.6, Section R.6.1.5, and ECHA's Practical guide "How to use and report (Q)SARs", section 3.2.

Therefore, the QSAR adaptation does not meet any of the cumulative conditions of Annex XI, Section 1.3.

B. Your QSAR predictions were performed on source substances, adapting the information in accordance with Annex XI, Section 1.5:

- In vitro mutations in bacteria (study i), prediction with dithiocarbonic acid O-ethyl ester (EC 205-780-8), study ii), predictions with sodium O-ethyl dithiocarbonate (EC 205-440-9) and sodium O-isobutyl dithiocarbonate (EC 246-805-2), and study iii), predictions for sodium ethyl xanthate (EC 205-440-9), sodium isopropyl xanthate (EC 205-443-5) and sodium isobutyl xanthate (EC 246-805-2))
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (prediction with dithiocarbonic acid O-ethyl ester (EC 205-780-8))
- In vitro mutations in mammalian cells (predictions with dithiocarbonic acid O-ethyl ester (EC 205-780-8))
- Screening study for reproductive/developmental toxicity (study i), ii) and iii), prediction with dithiocarbonic acid O-ethyl ester (EC 205-780-8), study iv), predictions with O-isopropyl hydrogen dithiocarbonate (EC 205-441-4), potassium O-ethyl dithiocarbonate (EC 205-439-3), potassium O-isobutyl dithiocarbonate (EC 235-837-2), sodium O-ethyl dithiocarbonate (EC 205-440-9), sodium O-isobutyl dithiocarbonate (EC 246-805-2), sodium O-isopropyl dithiocarbonate (EC 205-443-5), study v), prediction with sodium O-isobutyl dithiocarbonate (EC 246-805-2))

As explained in Section 1 of this Appendix, your adaptation according to Annex XI, Section 1.5 is rejected.

Therefore, QSAR modelling results results based on information on read-across are not adequate for classification and labelling and/or risk assessment.

ECHA's Conclusion

The adaptation you provided does not fulfil the criteria specified in Annex XI, Section 1.3. and it is therefore rejected.

In your comments to the draft decision you indicated your agreement to the draft decision and stated that "*QSAR on its own is not sufficient and that certain laboratory studies will be needed*".

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

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

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- 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.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- 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.)

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

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

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

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

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

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

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

1. Reliability of the read across approach

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

2. Reliability of the QSAR information

Section 2 of the present Appendix identifies deficiencies of the QSARs used in your dossier. These findings apply equally to the sources of information relating to QSARs submitted under your weight of evidence adaptations.

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

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

1. Surface tension

Surface tension is a standard information requirement in Annex VII to REACH (Section 7.6).

You have provided the following information for this endpoint:

i. An adaptation: "This endpoint is waived in accordance with Column 2 of Annex VII of the REACH Regulation as the substance is a solid at room temperature; the endpoint is not relevant".

ECHA has evaluated this information and identified the following issue(s):

According to Column 2 of Annex VII, Section 7.6, Surface tension, study only need to be conducted if i) based on structure, surface activity is expected or can be predicted, or ii) surface activity is a desired property of the material. If the water solubility is below 1 mg/l at 20 °C the test does not need to be conducted.

ECHA cannot relate your adaptation statement to any Column 2 adaptation for this endpoint. In addition, based on the structure of the Substance, surface activity can be expected, because the Substance has hydrophilic and lipophilic moieties.

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

2. In vitro gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is a standard information requirement in Annex VII to REACH.

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

You have provided the following sources of information to support your adaptations:

i) QSAR in vitro mutagenicity (Ames test) prediction (2012) on source substance dithiocarbonic acid O-ethyl ester (EC 205-780-8)
ii) QSAR prediction for carcinogenicity and mutagenicity (2008) on source substances sodium O-ethyl dithiocarbonate (EC 205-440-9) and sodium O-isobutyl dithiocarbonate (EC 246-805-2)
iii) Lazy Structure- Activity Relationships (2012) on source substances sodium O-ethyl dithiocarbonate (EC 205-440-9), sodium O-isopropyl dithiocarbonate (EC 205-443-5) and sodium O-isobutyl dithiocarbonate (EC 246-805-2)
iv) In vitro mutagenicity (Ames test) (1996) on source substance dithioxomethane (EC 200-843-6)
v) In vitro mutagenicity (Ames test) (1980) on source substance dithioxomethane (EC 200-843-6)

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

As explained in Section 3 of the Appendix common to several requests, the weight of evidence must fulfill 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.

For this endpoint your study needs to have adequate and reliable coverage of the key

parameters foreseen to be investigated in an OECD TG 471 test. The key parameter investigated by this test is detection and quantification of gene mutations (base pairs, substitution or frame shift) in cultured bacteria including data on the number of revertant colonies.

The provided studies investigate the above mentioned key parameter. Therefore, they provide information that would contribute to the conclusion on this key parameter.

However, the reliability of the sources of information is significantly affected by the deficiencies identified in Section 3 of the Appendix on Reasons common to several requests.

Taken together, even if these sources of information provide information on the key parameter, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

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

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

3. 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 the information requirement by using weight of evidence according to Annex XI, Section 1.2. In support of your adaptation, you have provided the following sources of information:

i. OECD TG 202 on source substance sodium O-ethyl dithiocarbonate (EC 205-440-9) ([redacted] 1988)
ii. OECD TG 202 on source substance sodium O-ethyl dithiocarbonate (EC 205-440-9) (Australian Government publishing Service, Cambera 1995)
iii. OECD TG 202 on source substance sodium ethyl dithiocarbonate ([redacted] 1979)

As explained in Section 3 of the Appendix on Reasons common to several requests, the weight of evidence must fulfill 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.

We have assessed this information and identified the following issues:

To fulfil the information requirement, normally a study according to OECD TG 202, and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test, must be provided. The key parameter investigated by this test is the inmobilisation of aquatic invertebrates.

All the sources of information you provided investigate the above mentioned key parameter. Therefore, they provide information that would contribute to the conclusion on this key parameter.

However, the reliability of these sources of information is significantly affected by the deficiencies identified in Section 3 of the Appendix on Reasons common to several requests.

In addition, the reliability of the source of information is also affected by the following issue.

The validity criteria of the OECD TG 202 indicate that:

i. the percentage of immobilised daphnids must be ≤ 10% at the end of the test in the controls
ii. the analytical measurement of test concentrations must be conducted
iii. the concentrations of the test material have to be measured at least at the highest and lowest test concentration, at the beginning and end of the test
iv. 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)

However:

i. the inmobilisation in the control(s) at the end of the test the studies were not provided in any of the studies
ii., iii and iv. no analytical measurement of test concentrations for any of the studies were provided.

Therefore, validity criteria are not fulfilled.

Taken together, even if these sources of information provide information on the key parameters, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

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

Study design

The Substance could be difficult to test due to the reported technical function of being a flotation agent in the CSR, which could mean the substance to have surface active properties. 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.

4. 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 the information requirement by using weight of evidence according to Annex XI, Section 1.2. In support of your adaptation, you have provided the following sources of information:

i. OECD TG 201 on source substance sodium ethyl dithiocarbonate ([redacted] 1979)
ii. OECD TG 201 on source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2) (IUCLID database, 2000)
iii. OECD TG 201 on source substance sodium ethyl dithiocarbonate (CESARS)
iv. OECD TG 201 on source substance carbon disulphide (EC 200-843-6) (IUCLID database, 1985)
v. OECD TG 221 on source substance sodium ethyl dithiocarbonate ([redacted] 1979)

As explained in Section 3 of the Appendix on Reasons common to several requests, the weight of evidence must fulfill 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.

We have assessed this information and identified the following issues:

To fulfil the information requirement, normally a study according to OECD TG 201 or 221, and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test, must be provided. The key parameter investigated by these tests is growth rate of algal cultures or of *Lemna sp*.

All the sources of information you provided investigate the above mentioned key parameters. Therefore, they provide information that would contribute to the conclusion on this key parameter.

However, the reliability of these sources of information is significantly affected by the deficiencies identified in Section 3 of the Appendix on Reasons common to several requests.

In addition, the reliability of the source of information is also affected by the following issues.

i. The validity criteria of the OECD TG 201 indicate that:

- 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* and *Desmodesmus subspicatus*. For other less frequently tested species, the value is ≤ 10%.

However, none of the studies following OECD TG 201 in your registration dossier provides:

- section-by-section growth rates in the control cultures;
- the initial biomass and the biomass at the end of the test
- the mean coefficient of variation for section-by-section specific growth, and
- the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures .

ii. Similarly, the validity criteria of the OECD TG 221 indicate that:

- exponential growth in the control cultures is observed over the entire duration of the test;
- An approximately 7-fold increase in biomass is observed in the control cultures by the end of the test.

However, none of the studies following OECD TG 221 in your registration dossier provide growth rates in the control cultures and the initial biomass and the biomass at the end of the test.

iii. Besides, the conditions of exposure in OECD TG 201 and 221 specify that the concentrations of the test material have to be measured at least at the highest and lowest test concentration (plus at a concentration around the expected EC_{50} in OECD TG 201), at the beginning and end of the test. It indicates further that 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. OECD TG 201 specifies further that "for volatile, unstable or strongly adsorbing test substances, additional samplings for analysis at 24 hour intervals is required."

However, none of the tests submitted include analytical monitoring data. This is essential, as the the Substance is a flotation agent, which could mean the substance has surface active properties and surface active substances are included as difficult to test chemicals in OECD GD 23.

Therefore, validity criteria is not fulfilled for any of the provided studies based on OECD TG 201 and 221.

Therefore, the requirements of OECD TG 201 nor 221 are not met.

Taken together, even if these sources of information provide information on the key parameters, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated by the required study. Therefore, your adaptation is rejected and 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 Section A.3.

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 a standard information requirement in Annex VIII to REACH.

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

In support of your adaptation you have submitted a QSAR adaptation of *in vitro* mammalian chromosome aberration test (similar to OECD TG 473, 2012) on source substance dithiocarbonic acid O-ethyl ester (EC 205-780-8).

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

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

You have only provided one source of information.

Irrespective of this deficiency, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided sources of information and found the following deficiency.

The reliability of the source of information is significantly affected by the deficiencies identified in Sections 1, 2 and 3 of the Appendix common to several requests.

Therefore your adaptation according to Annex XI, Section 1.2 is rejected and the information requirement is not fulfilled.

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 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.

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

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

The result of the requests for information in section 2 of Appendix A and section 1 of this Appendix B will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

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

In support of your adaptation, you have provided a QSAR adaptation of in vitro mammalian cell gene mutation test (similar to OECD TG 476, 2012) on source substance dithiocarbonic acid O-ethyl ester (EC 205-780-8).

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

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

You have only provided one source of information.

Irrespective of this deficiencies, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided source of information and found the following deficiency.

The reliability of the source of information is significantly affected by the deficiencies identified in Sections 1, 2 and 3 of the Appendix common to several requests.

Therefore your adaptation according to Annex XI, Section 1.2 is rejected and the information requirement is not fulfilled.

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. Short-term repeated dose toxicity (28 days)

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII (Section 8.6.1.) to REACH.

You have adapted the standard information requirement mentioned above using a Weight of Evidence under Annex XI, Section 1.2 of REACH.

You have provided the following sources of information:

i) Subchronic toxicity study (1966) in rat on source substance potassium O-butyl dithiocarbonate (EC 212-808-2)
ii) Handbook reference (2010) relevant to analogue substance potassium O-ethyl dithiocarbonate (EC 205-439-3), RL 3
iii) Subacute toxicity study (1996) on source substance dithioxomethane (EC 200-843-6)
iv) Subacute toxicity studies (1995) in mouse on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5)
v) Subacute toxicity studies (1995) in rat on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5)
vi) Subacute toxicity studies (1995) in rabbit on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5)
vii) Subacute toxicity studies (1995) in dog on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5)
viii) Repeated dose toxicity study (1996) on source substance dithioxomethane (EC 200-843-6)

ix) Subacute toxicity study (1996) on source substance dithioxomethane (EC 200-843-6)
x) Subacute toxicity study (1996) on source substance dithioxomethane (EC 200-843-6)

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

As explained in Section 2 of the Appendix common to several requests, the weight of evidence adaptation must fulfill 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.

For this endpoint your study needs to have adequate and reliable coverage of the key parameters foreseen to be investigated in an OECD TG 407 test, which are information on systemic toxicity in intact, non-pregnant and young adult males and females from: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity.

The provided studies investigate the above mentioned key parameters. Therefore, they provide information that would contribute to the conclusion on this key parameters.

However, the reliability of these studies are significantly affected by the deficiencies identified in Section 2 of the Appendix on Reasons common to several requests.

In addition, ECHA agrees that study ii) is unreliable, while the reliability of the other sources of information for this endpoint is also affected by the following issue:

The conditions of this test guideline include
- testing of at least three dose levels and a concurrent control
- 5 female and 5 male animals should be used at each dose level (including control group)
- examination of the animals for histopathology (including thyroid gland/ thyroid hormone measurements), and pathology of sexual (male and female) organs, full detailed gross necropsy and subsequent histopathology of both types tissues

The studies i), iv), v), vi) and vii) were conducted with less than three dose levels, while for studies iii), viii), ix) and x) there is no information on the number doses.

The studies i), iv), v), vi) and vii) were conducted with less than 5 animals per sex per test dose group (only male animals investigated), while for studies i), iii), viii), ix) and x) there is no information on the number of animals.

For studies i), iii), iv), v), vi), vii), viii), ix) and x) there is no information if the above toxicological examinations were included.

Therefore, the study conditions are not fulfilled and the provided studies cannot be considered reliable sources of information that could contribute to the conclusion on the key parameters investigated by the required study.

Taken together, even if these sources of information provide information on the key parameters, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous

property foreseen to be investigated by the required study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

Information on study design

Referring to the criteria provided in Annex VIII, Section 8.6.1, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because even though the substance is reported to occur as a dust with a significant proportion (>1% on weight basis) of particles of inhalable size (MMAD < 50 µm), no oral repeated dose toxicity study is available to evaluate systemic toxicity following oral administration.

REACH Annex VIII, Section 8.6.1. refers to short-term repeated dose toxicity (28 days), which can be tested by the oral route according to the test methods OECD TG 407 or 422. REACH Annex VIII, Section 8.7.1. refers to screening studies for reproductive/ developmental toxicity according to the test methods OECD TG 421 or 422. As pointed out below in section B.4 of this decision, the information provided under Annex VIII, Section 8.7.1. does not fulfil the information requirement for reproductive/developmental toxicity and therefore there is an information gap. To prevent unnecessary animal testing, an OECD TG 422 study is more appropriate to fulfil the information requirements of both Sections 8.6.1. and 8.7.1. of Annex VIII, as it provides initial information on reproductive/developmental toxicity and on short-term repeated dose toxicity.

Therefore the study must be performed according to the OECD TG 422, in rats and with oral administration of the Substance.

4. 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 Weight of Evidence under Annex XI, Section 1.2 of REACH.

You have provided the following sources of information:

i.) AP1-AP7 FDA Sperm Toxicity set, 2012; QSAR prediction on source substance dithiocarbonic acid O-ethyl ester (EC 205-780-8)
ii.) AN1-AN9 FDA Reproductive toxicity in females set, 2012; QSAR prediction on source substance dithiocarbonic acid O-ethyl ester (EC 205-780-8)
iii.) AO1-AO7 FDA Reproductive toxicity in adult males set, 2012; QSAR prediction on source substance dithiocarbonic acid O-ethyl ester (EC 205-780-8)
iv.) QSARs for predicting effects relating to reproductive toxicity, 2008; QSAR predictions on source substances O-isopropyl hydrogen dithiocarbonate (EC 205-441-4), potassium O-ethyl dithiocarbonate (EC 205-439-3), potassium O-isobutyl dithiocarbonate (EC 235-837-2), sodium O-ethyl dithiocarbonate (EC 205-440-9), sodium O-isobutyl dithiocarbonate (EC 246-805-2), sodium O-isopropyl dithiocarbonate (EC 205-443-5), RL 3
v.) Predicted Values-Estrogen Receptor Binding Affinity; QSAR prediction on source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2)

As explained in Section 3 of the Appendix common to several requests, the weight of evidence adaptation must fulfill 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.

For this endpoint your study needs to have adequate and reliable coverage of the key parameters foreseen to be investigated in a OECD TG 422 study, wich are 1) sexual function and fertility, 2) toxicity to offspring, and 3) systemic toxicity.

The provided sources of information investigate the above mentioned key parameters. Therefore, they provide information that would contribute to the conclusion on this key parameter.

However, the reliability of the sources of information is significantly affected by the deficiencies identified in Section 3 of the Appendix on Reasons common to several requests.

In addition, ECHA agrees that study iv) is unreliable.

Taken together, even if these sources of information provide information on the key parameters, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

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

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[9] administration of the Substance.

Information on study design

When there is no information available neither for the 28-day repeated dose toxicity endpoint (EU B.7, OECD TG 407) (as explained above under section 3.), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1.[10]

A study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral[11] administration of the Substance.

5. 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 weight of evidence according to Annex XI, Section 1.2. In support of your adaptation, you have provided the following sources of information:

[9] ECHA Guidance R.7a, Section R.7.6.2.3.2.
[10] ECHA Guidance, Section R.7.6.2.3.2., pages 484 to 485 of version 6.0 – July 2017. (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf)
[11] ECHA Guidance R.7a, Section R.7.6.2.3.2.

i. EPA OTS 797.1400 on source substance Sodium ethyl dithiocarbonate (Ministry of Environment, Canada 1977)
ii. EPA OTS 797.1400 on source substance sodium O-isopropyl dithiocarbonate (EC 205-443-5) (Ministry of Environment, Canada 1977)
iii. EPA OTS 797.1400 on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) on *Pimephales promelas* (Ministry of Environment, Canada 1977)
iv. EPA OTS 797.1400 on source substance sodium O-isopropyl dithiocarbonate (EC 205-443-5) on *Notropis atherinoides* (Ministry of Environment, Canada 1977)
v. OECD TG 203 on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) (Australian Government, Camberra 1995), LC50(96h)= 12 mg/L
vi. OECD TG 203 on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) (Australian Government, Camberra 1995), LC50(24h)= 25 mg/L ; LC100 (48h)= 25 mg/L
vii. OECD TG 203 on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) (Australian Government, Camberra 1995), LC50(48h)= 18 mg/L ; LC0 (48h)= 6 mg/L
viii. OECD TG 203 on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) (Australian Government, Camberra 1995), LC50(48h)= 70-80 mg/L
ix. OECD TG 203 on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) on *Notropis atherinoides* (Australian Government, Camberra 1995)
x. OECD TG 203 on source substance sodium O-isobutyl dithiocarbonate (EC EC 246-805-2) (CESARS 1976)
xi. OECD TG 203, on source substance potassium O-ethyl dithiocarbonate (EC 205-439-3) (Webb et al., 1976), LC50(96h)= 1.5 mg/L
xii. OECD TG 203 on source substance potassium O-ethyl dithiocarbonate (EC 205-439-3) (Webb et al., 1976), LC50(96h)= 2 mg/L
xiii. OECD TG 203 on source substance potassium O-ethyl dithiocarbonate (EC 205-439-3) (Webb et al., 1976), LC50(96h)= 52 mg/L
xiv. OECD TG 203 on source substance potassium O-ethyl dithiocarbonate (EC 205-439-3) (Webb et al., 1976), LC50(96h)= 9.8 mg/L
xv. OECD TG 203 on source substance potassium O-ethyl dithiocarbonate (EC 205-439-3) on *Cyprinus carpio* (Webb et al., 1976), LC50(96h)= 166 mg/L
xvi. OECD TG 203 on source substance potassium o-isobutyl dithiocarbonate (EC 235-837-2) (IUCLID database, 2000)
xvii. OECD TG 203 on source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2) (Webb et al., 1976), LC50(96h)= 70 mg/L
xviii. OECD TG 203 on source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2) (Webb et al., 1976), LC50(96h)= 10-100 mg/L
xix. OECD TG 203 on source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2) (Ledudc et al., 1973)
xx. OECD TG 203 on source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2) (Zhang & Yin, 1986)
xxi. OECD TG 203 on source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2) (US EPA 1973), LC50(96h)= 18-20 mg/L
xxii. OECD TG 203 on source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2) (US EPA 1973), LC50(96h)= 180 mg/L
xxiii. OECD TG 203 on source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2) (US EPA 1973), LC50(96h)= 10 mg/L

As explained in Section 3 of the Appendix on Reasons common to several requests, the weight of evidence must fulfill 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.

We have assessed this information and identified the following issues:

To fulfil the information requirement, normally a study according to OECD TG 203, and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test , must be provided. The key parameter investigated by this test is mortality of the juvenile fish.

All the sources of information you provided investigate the above mentioned key parameter. Therefore, they provide information that would contribute to the conclusion on this key parameter.

However, the reliability of these sources of information is significantly affected by the deficiencies identified in Section 3 of the Appendix on Reasons common to several requests.

In addition, the reliability of the source of information is also affected by the following issue.

The validity criteria of the OECD TG 203 and for EPA OTS 797.1400 include that mortality in the control(s) needs to be is ≤ 10% (or one fish, if fewer than 10 control fish are tested) at the end of the test and the analytical measurement of test concentrations must be conducted.

However, the mortality in the control(s) at the end of the test the studies were not provided and there were no analytical measurement of test concentrations for any of those studies.

Therefore, validity criteria is not fulfilled.

Taken together, even if these sources of information provide information on the key parameters, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated by the required study. Therefore, your adaptation is rejected and 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 could be difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Section A.3.

Appendix C: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. Test methods, GLP requirements and reporting

1. Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

2. Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[12].

B. Test material

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 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.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[13].

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

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

A. Testing strategy for aquatic toxicity testing

You are advised to consult ECHA Guidance R.7b, (Section R.7.8.5) which describes the Integrated Testing Strategy, to determine the sequence of aquatic toxicity tests and testing needed.

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 17 January 2020.

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

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

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix F: List of references - ECHA Guidance[14] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[15]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[15]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[16]

[14] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[15] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[16] 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 the corresponding information requirements applicable to them

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.