~~Confidential~~

Helsinki, 10 November 2021

Addressees
Registrant(s) of Joint Submission PIBX as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
03/12/2012

Registered substance subject to this decision ("the Substance")
Substance name: Potassium O-isobutyl dithiocarbonate
EC number: 235-837-2
CAS number: 13001-46-2

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 ***15 February 2024***.

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

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

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

2. Skin sensitisation (Annex VII, Section 8.3.; test method:

   i. *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (EU B.71/OECD TG 442E)(Annex VII, Section 8.3.1.); and
   ii. Only if the *in vitro/in chemico* test methods specified under point 2.i.) are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429);

3. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. / OECD TG 471) Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202)

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

5. 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. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days) requested below (Annex VIII, Section 8.6.1.)

4. 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

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

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

How to comply with your information requirements

To comply with your information requirements you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must

also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

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

Appeal

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

Failure to comply

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

Authorised[1] under the authority of 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.)
- Skin sensitisation (Annex VII, Section 8.3)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- 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.)
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

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 / CAS 75-15-0 / EC 200-843-6

[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

2) 2-methylpropan-1-ol / 78-83-1 / 201-148-0
3) Potassium hydroxide / CAS 1310-58-3 / EC 215-181-3
4) Potassium isopropyl xanthate / CAS 140-92-1 / EC 205-441-4.
5) Potassium O-butyl dithiocarbonate / CAS 871-58-9 / EC 212-808-2
6) Potassium O-ethyl dithiocarbonate / CAS 140-89-6 / EC 205-439-3
7) Potassium O-hexyl dithiocarbonate / CAS 2720-76-5 / EC 220-331-6
8) Potassium O-pentyl dithiocarbonate / CAS 2720-73-2 / EC 220-329-5
9) Sodium dimethyldithiocarbamate / CAS 128-04-1 / EC 204-876-7)
10) Sodium O-ethyl dithiocarbonate / CAS 140-90-9 / EC 205-440-9
11) Sodium O-isobutyl dithiocarbonate / CAS 25306-75-6 / EC 246-805-2
12) Sodium O-isopropyl dithiocarbonate / CAS 140-93-2 / EC 205-443-5.
13) Sodium O-sec-butyl dithiocarbonate / CAS 36551-21-0 / EC 253-097-9
14) Zinc bis(dimethyldithiocarbamate) / CAS 137-30-4 / EC 205-288-3
15) Zinc bis(diethyldithiocarbamate) EC 238-270-9

as source substances and the Substance as target substance.

You have provided the following reasoning for the prediction of (eco)toxicological properties: and "*carbon disulphide is the major decomposition product of potassium amyl xanthate and it is therefore important to also consider the health and safety hazards of this substance. Carbon disulphide is readily given off when potassium amyl xanthate comes intocontact with water.* […] *Repeated exposure to carbon disulphide may cause long-term effects such as reproductive and CNSeffects."*

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)-15), 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.

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

a. Missing information on the formation of common compound

As indicated above, one of your read-across hypotheses (1) is based on the (bio)transformation of 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 hypotheses (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 Substance and the source 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 negative results are reported for equivalent studies conducted on source substances provided in your dossier. The analogue substance potassium isopentyl dithiocarbonate is also a xanthate substance, but no scientific reason was provided for

[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.

considering only other xanthate substances in your read-across justification for all (eco)toxicological endpoints.

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 studies

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

There are deficiencies discussed under Appendix A, sections 3, 4 and 5, Appendix B, sections 1 3 and 5, Appendix C, sections 1, 3 and 4.

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 indicate your intention to prepare a read-across category for the Substance and the analogue substances

807-374-1 Isoamyl xanthate
205-439-3 Potassium O-ethyl dithiocarbonate
205-443-5 Proxan-sodium
213-180-2 Potassium isopentyl dithiocarbonate
220-977-9 S-allyl O-pentyl dithiocarbonate
220-329-5 Potassium O-pentyl dithiocarbonate

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

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:

- short-term toxicity in fish
- long-term toxicity in fish
- short-term toxicity in aquatic invertebrates
- long-term toxicity in aquatic invertebrates
- toxicity in aquatic plants

For the ecotoxicity endpoints, you have provided estimated toxicity values for the endpoints derived with ECOSAR program. You have provided summaries of the predictions and the outcome of the predictions.

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.[7]

You have used ECOSAR v1.00. The Substance is an O-ester of a dithiocarbonate salt. Therefore, it has an ester group and it is a salt.

Based on the above, the Substance is not a neutral organic.

However, ECOSAR v1.00 does not recognise the Substance as ester group and salt but mislabels it as an neutral organic.

Therefore, the Substance does not fall within the applicability domain of the model for all endpoints mentioned above.

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

You have adapted the following standard information requirements by applying weight of

[7] 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.

evidence (WoE) adaptation in accordance with Annex XI, section 1.2:

- Skin sensitisation, in vitro/in chemico (Annex VII, Section 8.3.1.)
- 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.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Long-term toxicity testing on 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 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. <u>Reliability of the read across approach</u>

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. <u>Reliability of the QSAR information</u>

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: "Surface tension is not applicable to subtances that dissociate in aqueous solutions."

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. Skin sensitisation

Skin sensitisation is a standard information requirement in Annex VII, Section 8.3. to the REACH Regulation. Column 1 of Section 8.3. requires the registrants to submit information allowing a conclusion whether the substance is a skin sensitiser and whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), and risk assessment, where required.

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

In your comments to the draft decision you state that "*the study does not need to be conducted if the available information indicates that the substance should be classified for skin sensitisation or corrosivity*." ECHA notes the Substance has not been classified accordingly.

You have provided the following sources of information in support for your adaptation:

i) No guideline indicated, *in* vivo skin sensitisation test (1975) on source substance potassium hydroxide (EC 215-181-3)
ii) Local Lymph Node Assay (2010) on source substance dithioxomethane (EC 200-843-6)

In your comments to the draft decision you state that "*well-performed studies on PIAX (2012) and on SIBX (1978) where the substances are classified as sensitizer can be used as read across*."

In your comments you did not provide further supporting information.

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

Weight of evidence

As explained in Section 3 of the Appendix on Reasons 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 TG 442C, 442D and 442E, or 429 test. Skin sensitisation is an information requirement under Annex VII (Section 8.3.). Under Section 8.3., Column 1, the registrants must submit information allowing a conclusion whether the substance is a skin sensitiser and whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), and risk assessment, where required.

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.

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.

Adaptation based on skin sensitisation or corrosivity

In your comments to the draft decision you state that "*the study does not need to be conducted if the available information indicates that the substance should be classified for skin sensitisation or corrosivity*." You did not specifically claim an adaptation but your comments could be interpreted as an adaptation intention according to first indent of Annex VII, Section 8.3.1, Column 2.

We have assessed this information and identified the following issue:

Under Annex VII, Section 8.3, Column 2, first indent, the study(ies) does not need to be conducted if the substance is classified as skin corrosion (Category 1).

The Substance has not been classified for corrosivity.

Therefore, the adaptation is rejected.

It should also be noted that this legal provision does not allow to adapt this information requirement in case a substance is classified as skin sensitising (Category 1). Column 1 specifically requires information allowing a conclusion not only on whether a substance is a skin sensitiser but also on whether it can be presumed to have the potential to produce significant sensitisation in humans (Category 1A).

To fulfil the information requirement for the Substance for skin sensitisation, *in vitro/in*

chemico studies (OECD TG 442C, 442D and 442E) are considered suitable. In case *in vitro/in chemico* methods are not suitable for the Substance or the results cannot be used for classification and risk assessment an *in vivo* skin sensitisation study (OECD TG 429) must be performed.

3. 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) *In vitro* gene mutation study in bacteria (1992) on source substance dithioxomethane (EC 200-843-6)
ii) *In vitro* gene mutation study in bacteria (1985) on source substance 2-methylpropan-1-ol (EC 201-148-0)
iii) *In vitro* gene mutation study in bacteria (1988) on source substance 2-methylpropan-1-ol (EC 201-148-0)
iv) No guideline indicated, gene mutation study in bacteria (1992) on source substance potassium hydroxide (EC 215-181-3)

In your comments to the draft decision you stated that "*well-performed study on PIAX (2012) was submitted in its registration dossier where the test substance did not exert mutagenic activity both in presence and absence of metabolic activation and therefore this substance can be used as read across*."

In your comments you did not provide further supporting information.

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

Weight of evidence

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.

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 i) iv) 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 sources of information is also affected by the following issues.

The conditions of OECD TG 471 specify that:

- The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S.* typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101)
- The mean number of revertant colonies per plate must be reported for the treated doses and the controls.

The source of information i) you have provided did not include the required fifth strain, S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101).

The source of information iv) you have provided did not include the three required strains of *S. typhimurium* (TA98; TA100; TA1535)).

The source of information i) you have provided did not include data on the number of revertant colonies per plate for the treated doses and the controls.

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.

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

4. 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. ECOSAR estimation on the Substance on Mysid shrimp
ii. ECOSAR estimation on the Substance on Daphnids
iii. OECD TG 202 on source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2) ([redacted] 1988)
iv. OECD TG 202 on source substance sodium O-isopropyl dithiocarbonate (EC 205-443-5) ([redacted] 1988)
v. OECD TG 202 on source substance sodium O-sec-butyl dithiocarbonate (EC 253-097-9) ([redacted] 1973)
vi. OECD TG 202 on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) ([redacted] 1988)
vii. OECD TG 202 on source substance potassium O-ethyl dithiocarbonate (EC 205-439-3) ([redacted] 1973)
viii. OECD TG 202 on source substance carbon disulphide ([redacted] 1985)

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 tests were not provided for any study
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 is difficult to test due to the use as a surface agent. 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.

5. Growth inhibition study aquatic plants

Growth inhibition study aquatic plantsGrowth 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 carbon disulphide (EC 200-843-6) ([redacted] 1985)
ii. ECOSAR estimate on the Substance
iii. DIN 38412, Part 9 on source substance 2-methylpropan-1-ol (EC 201-148-0) ([redacted] 1990)
iv. OECD TG 221 on sodium O-isobutyl dithiocarbonate (EC 246-805-2) ([redacted] 1988)
v. OECD TG 221 on source substance sodium O-ethyl dithiocarbonate (EC 205-440-9) ([redacted] 1988)

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 based on these studies include analytical monitoring data. This is essential, as the the Substance used as a surface agent, 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.

iv. Although you do not explicitly claim an adaptation, ECHA understands that sources of information (iii.) was submitted in order to meet the information requirement by means of adaptation according to Annex XI, Section 1.1.2. This adaptation rule enables registrants to claim that the data from experiments not carried out according to GLP or the test methods referred to in Article 13(3) can be considered equivalent to data generated by those test methods.

The adaptation rule in Annex XI, Section 1.1.2. imposes a number of cumulative conditions for an adaptation to be valid, in particular: Adequate and reliable documentation of the study is provided.

The DIN 38412, part 9 is not one of the guidelines listed in ECHA's Guidance R7b as an acceptable alternative to the OECD TG 201/ EU Method C.3 standard methods under Article 13(3) of REACH.

You have not provided adequate and reliable documentation in a form of a robust study

summary, as required by Article 10(a)(vii) and Article 3(28). The study summary performed based on DIN 38412, part 9 is poorly reported. For example, little information is given on details on test solution (pH, test temperature and concentration range, and the dossier contains no information on the controls.

The provided information does not allow establishing whether validity criteria would be fulfilled in the absence of information on control cultures and detailed test solution information.

Therefore, you have not demonstrated the validity of the study on the basis of the current information.

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.4.

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.

You have provided the following sources of information:

i) *In vitro* mammalian cell micronucleus test (2002) on source substance 2-methylpropan-1-ol (EC 201-148-0)
ii) *In vitro* chromosome aberration test (1989) on source substance zinc bis(dimethyldithiocarbamate) (EC 205-288-3)
iii) *In vivo* mammalian erythrocyte micronucleus test (2000) on source substance 2-methylpropan-1-ol (EC 201-148-0)
iv) *In vivo* chromosome aberration assays in spermatogonia and bone marrow (1992) on source substance zinc bis(dimethyldithiocarbamate) (EC 205-288-3)
v) *In vivo* chromosome aberration assays in bone marrow (1992) on source substance zinc bis(dimethyldithiocarbamate) (EC 205-288-3)
vi) *In vivo* mammalian erythrocyte micronucleus test (1992) on source substance zinc bis(dimethyldithiocarbamate) (EC 205-288-3)
vii) *In vivo* mammalian erythrocyte micronucleus test (1992) on source substance dithioxomethane (EC 200-843-6)
viii) A reference to a scientific review on source substance dithioxomethane (EC 200-843-6) (Canadian Environmental Protection Act 2000).

In your comments to the draft decision you stated that "*well-performed study on PIAX (2012) was submitted in its registration dossier where the test substance did not induce chromosome aberrations both in presence and absence of metabolic activation and therefore this substance can be used as read across*."

In your comments you did not provide further supporting information.

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

Weight of evidence

As explained in Section 3 of the Appendix on Reasons 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 473 or 487 test. The key parameter investigated by these tests is detection and quantification of structural or numerical chromosomal aberrations in cultured mammalian cells including data on the cytotoxicity and the frequency of cells with chromosomal aberrations or micronuclei.

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, the reliability of the sources of information for this endpoint is also affected by the following issue:

Annex XI, Section 1.2 requires adequate and reliable documentation.

You describe information source viii) as a "*review of a large series of publications on studies in which a wide array of methods was applied*", without further details on conducted studies. This does not qualify as adequate and reliable documentation.

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.

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.

You have provided the following sources of information:

i) *in vitro* mammalian cell gene mutation test (2002a) on source substance 2-methylpropan-1-ol (EC 201-148-0)
ii) *in vitro* mammalian cell gene mutation test (2002b) on source substance 2-methylpropan-1-ol (EC 201-148-0)

In your comments to the draft decision you stated that "*well-performed study on PIAX (2012) was submitted in its registration dossier where the test substance is positive without metabolic activation and ambiguous with metabolic activation but the substance is not considered to be mutagenic in humans according to this in vitro gene mutation in mammalian cells test and therefore this substance can be used as read across*."

In your comments you did not provide further supporting information.

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

Weight of evidence

As explained in Section 3 of the Appendix on Reasons 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 476 or 490 test. The key parameter investigated by these tests is detection and quantification of gene mutations (point mutations, frame-shift mutations, small deletions, etc.) including data on the frequency of mutant colonies in cultured mammalian cells (in vitro) or mutant frequency for each tissue in mammals (in vivo).

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

However, the reliability of this study 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 for this endpoint is also affected by the following issue:

As indicated above, one of your read-across hypotheses is based on the (bio)transformation of the category members to a common compound(s). In this context, information on all hydrolysis products is necessary to assess the impact of the exposure to each of these in order to predict the properties of the Substance.

You have provided information on the formation of only one metabolite (2-methylpropan-1-ol); you have not provided source studies for all metabolites that are likely to be formed.

In the absence of information on all (bio)transformation products that are likely to be formed, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

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.

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. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days)

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII to REACH. This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 of Annex VIII or a general adaptation rule under Annex XI.

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) Subchronic toxicity study (1966) in rat on source substance potassium O-butyl dithiocarbonate (EC 212-808-2);
ii) Subchronic toxicity study (1995) in rat on source substance potassium sodium dimethyldithiocarbamate (EC 204-876-7);
iii) Subacute toxicity studies (1976) in rat, rabbit and mouse on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5);
iv) Subacute toxicity study (1989) in rabbit on source substance zinc bis(dimethyldithiocarbamate) (EC 205-288-3);

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

As explained in Section 3 of the Appendix on Reasons 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. The key parameters investigated by this test is 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 key parameters. Therefore, they provide information that would contribute to the conclusion on this key parameter.

However, the reliability of this study 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 sources of information iii) and iv) for this endpoint are also affected by the following issue (reliability of the sources of information i) and ii) are addressed under Section C.1):

The conditions of OECD TG 407 specify:

- testing of at least three dose levels and a concurrent control
- at least 5 female and 5 male animals should be used at each dose level (including control group)
- dosing of the Substance daily for a period of 28 days until the scheduled termination

of the study

- histopathology (including thyroid gland/ thyroid hormone measurements), urinalysis, sensory reactivity to various stimuli and functional observations of the animals, and pathology of sexual (male and female) organs, full detailed gross necropsy and subsequent histopathology of both types tissues

The study iii) you have provided was conducted with less than three dose levels, and less than 5 animals per sex per test dose group (only male animals investigated).

The study iv) you have provided does not have the required exposure duration of 28 days.

The study iii) you have provided was conducted without the above listed toxicological investigations according to the information provided in the dossier.

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.

Column 2 of Annex VIII, Section 8.6.1. provides that an experimental study for this endpoint is not needed if a reliable sub-chronic (90 days) or chronic toxicity study is available.

The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see Section C.1). According to Column 2 of Annex VIII, Section 8.6.1., and to prevent unnecessary animal testing, a short term toxicity study (28 days) does not therefore need to be conducted.

Because you still must comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to submit a justification for the adaptation provided in Column 2 of that provision.

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

In your comments to the draft decision you state that "*only a waiver should be requested by ECHA*" and indicate your intention to conduct a prenatal developmental study and adapt the information requirement according to Annex VIII, Section 8.7.1, Column 2 fourth indent. ECHA acknowledges your intention and awaits further information. ECHA will evaluate the latest submission provided after the deadline of this decision.

You also emphasise in the comments to the draft decision the provisions of REACH "*information shall be generated whenever possible by means other than vertebrate animal*

tests, […] or from information from structurally related substances (grouping or read-across)." ECHA understands this as an intention to adapt the information requirement. It is in your discretion to generate and provide the necessary supporting information in order to justify any adaptation. If you do so, you are responsible for demonstrating the fulfilment of the specific requirements of Annexes VII-IX and/or the general requirements of Annex XI to REACH. ECHA will evaluate the latest submission provided after the deadline of this decision.

You have provided the following sources of information:

i.) One generation reproductive toxicity study in rat (1992) on source substance CS2 (EC 200-843-6)
ii.) Guideline not specified, study in rat (1984) on source substance CS2 (EC 200-843-6)
iii.) Two generation reproductive toxicity study in rat (1978) on source substance CS2 (EC 200-843-6)
iv.) Two generation reproductive toxicity study in rat (1996) on source substance Ziram (EC 205-288-3)

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

Weight of evidence

As explained in Section 3 of the Appendix on Reasons 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 421 or 422 study. The key parameter investigated by this test include the following key elements: 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 iii) is unassignable/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[8] administration of the Substance.

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

Comments to the draft decision

In your comments to the draft decision you refer to Annex VIII 8.7.1, Column 2 waiving possibility and state that "*only a waiver should be requested by ECHA.*" According to you "*ECHA has not taken this waiver into account since it requires this very pre-natal developmental toxicity be performed*." You furthermore indicate in the comments your intention to conduct a prenatal developmental study and adapt the information requirement according to Annex VIII, Section 8.7.1, Column 2 fourth indent.

You also emphasise the provisions of REACH that "*information shall be generated whenever possible by means other than vertebrate animal tests, […] or from information from structurally related substances (grouping or read-across).*"

A pre-natal developmental toxicity study does not provide all the information that a screening study would provide.

ECHA acknowledges the possibilities to waive the information requirement if the criteria of Annex VIII, Section 8.7.1, Column 2 fourth indent is met. However, the information provided in your dossier does not comply with REACH Regulation. Therefore, ECHA is requesting information. 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)*."

In any case, it is in your discretion to generate and provide the necessary supporting information in order to justify any adaptation. If you do so, you are responsible for demonstrating the fulfilment of the specific requirements of Annexes VII-IX and/or the general requirements of Annex XI to REACH. ECHA will evaluate the latest submission provided after the deadline of this decision.

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:

i. OECD TG 203 on source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2) ([redacted] 1976)
ii. OECD TG 203 on source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2) ([redacted] 1973)
iii. OECD TG 203 on source substance carbon disulphide (EC 200-843-6) ([redacted] 1985)
iv. ECOSAR estimation on the Substance on freshwater fish
v. ECOSAR estimation on the Substance on saltwater fish
vi. OECD TG 203 on source substance sodium O-sec-butyl dithiocarbonate (EC 253-097-9) ([redacted] 1976)
vii. OECD TG 203 on source substance sodium O-sec-butyl dithiocarbonate (EC 253-097-9) ([redacted] 1973)
viii. OECD TG 203, Weight of Evidence on potassium O-hexyl dithiocarbonate (EC 220-331-6) ([redacted] 1976)
ix. OECD TG 203 on source substance sodium O-isopropyl dithiocarbonate (EC 205-

443-5) ([redacted] 1974)
x. OECD TG 203 on source substance sodium O-isopropyl dithiocarbonate (EC 205-443-5) ([redacted] 1976)
xi. OECD TG 203 on source substance sodium O-isopropyl dithiocarbonate (EC 205-443-5) on *Ictalurus punctatus* ([redacted] 1986)
xii. OECD TG 203 on source substance sodium O-isopropyl dithiocarbonate (EC 205-443-5) on *Lepomis macrochirus* ([redacted] 1986)
xiii. OECD TG 203 on source substance O-isopropyl hydrogen dithiocarbonate (EC 205-441-4), ([redacted] 1976)
xiv. OECD TG 203 on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) ([redacted] 1976)
xv. OECD TG 203 on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) ([redacted] 1974)
xvi. OECD TG 203 on source substance potassium hydroxide (EC 215-181-3)([redacted] 1957)
xvii. OECD TG 203, Weight of Evidence on potassium O-ethyl dithiocarbonate (EC 205-439-3) ([redacted] 1976)
xviii. OECD TG 203, Weight of Evidence on potassium O-ethyl dithiocarbonate (EC 205-439-3) ([redacted] 1974)

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 sources of information is also affected by the following issue.

A. The validity criteria of the OECD TG 203 indicate 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 tests were not provided and there were no analytical measurement of test concentrations for any of those studies.

Therefore, validity criteria is not fulfilled.

You have assigned the endpoint study record xvi. ([redacted] 1957) with a reliability 3, and further explanated it to be "*due to documentation being insufficient for assessment. The dilution water was turbid, which could influence the buffer (neutralization) capacity of the*

water. This is a significant methodological deficiency." ECHA agrees with your assessment. Therefore, this study record is not reliable.

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.

In your comments to the draft decision you state that "ECHA should not request studies be performed but only demand the respective missing information." You further emphasise the provisions of REACH that "information shall be generated whenever possible by means other than vertebrate animal tests, […] or from information from structurally related substances (grouping or read-across)."

Under Article 41 of REACH, ECHA may request 'any information needed to bring the registration(s) into compliance with the relevant information requirements'. ECHA is thus empowered to request a study as it qualifies as such needed information.

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)."

It is in your discretion to generate and provide the necessary supporting information to justify any adaptation. If you do so, you are responsible for demonstrating the fulfilment of the specific requirements of Annexes VII-IX and/or the general requirements of Annex XI to REACH. ECHA will evaluate the latest submission provided after the deadline of this decision.

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 Section A.4.

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

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

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

You have adapted this information requirement by using 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) Subchronic toxicity study (1995) in rat on source substance potassium sodium dimethyldithiocarbamate (EC 204-876-7);
iii) Subacute toxicity studies (1976) in rat, rabbit, mouse and dog, on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5);
iv) Subacute toxicity study (1989) in rabbit on source substance zinc bis(dimethyldithiocarbamate) (EC 205-288-3);

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

Weight of evidence

As explained in Section 3 of the Appendix on Reasons 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 408 test. The key parameters investigated by this test is 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 parameter.

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

In addition to the reliability issues raised under B.3, the reliability of the sources of information for this endpoint are also affected by the following issue:

The conditions of OECD TG 408 include:

- testing of at least three dose levels and a concurrent control
- At least 10 female and 10 male animals should be used at each dose level (including control group)
- dosing of the Substance daily for a period of 90 days until the scheduled termination of the study
- histopathology (including thyroid gland/ thyroid hormone measurements), urinalysis, sensory reactivity to various stimuli and functional observations of the animals, and pathology of sexual (male and female) organs, full detailed gross necropsy and subsequent histopathology of both types tissues

The study i) you have provided was conducted with less than three dose levels, and less than 10 animals per sex per test dose group (only male animals investigated), while the number of investigated male animals is not reported.

The studies iii) and iv) you have provided do not have the required exposure duration of 90 days.

The study i) you have provided was conducted without the above listed toxicological investigations according to the information provided in the dossier.

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.

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017) Chapter R.7a, Section R.7.5.4.3 - is the most appropriate route of administration. More specifically, 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. Hence, the test shall be performed by the oral route using the test method OECD TG 408.

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

Comments to the draft decision

In your comments to the draft decision you state that "*ECHA should not request studies be performed but only demand the respective missing information*." You further emphasise the provisions of REACH that "*information shall be generated whenever possible by means other than vertebrate animal tests, […] or from information from structurally related substances (grouping or read-across).*"

Under Article 41 of REACH, ECHA may request 'any information needed to bring the registration(s) into compliance with the relevant information requirements'. ECHA is thus empowered to request a study as it qualifies as such needed information.

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)."*

It is in your discretion to generate and provide the necessary supporting information in order to justify any adaptation. If you do so, you are responsible for demonstrating the fulfilment of the specific requirements of Annexes VII-IX and/or the general requirements of Annex XI to REACH. ECHA will evaluate the latest submission provided after the deadline of this decision.

2. Pre-natal developmental toxicity study in one species

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

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

You have provided the following sources of information:

i.) prenatal developmental toxicity study in rabbit (1991) on source substance CS2 (EC 200-843-6)
ii.) prenatal developmental toxicity study in rat (1984a) on source substance CS2 (EC 200-843-6)
iii.) prenatal developmental toxicity study in rabbit (1984b) on source substance CS2 (EC 200-843-6)
iv.) guideline not specified, study in rat (1983) on source substance CS2 (EC 200-843-6)
v.) guideline not specified, study in rat (2000) on source substance CS2 (EC 200-843-6)
vi.) guideline not specified, study in rat (1989) on source substance CS2 (EC 200-843-6)
vii.) guideline not specified, study in rat (1984) on source substance zinc bis(diethyldithiocarbamate (EC 238-270-9)
viii.) guideline not specified, study in rat (1999), 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 on Reasons 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 414 study in a first species. The key investigations of this study cover the following aspects: 1) prenatal developmental toxicity, 2) maternal toxicity, and 3) maintenance of pregnancy.

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 studies iv., v. and vi. are unassignable/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 PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[9] administration of the Substance.

In your comments on the draft decision you provide the same information for this endpoint as for request C.1. ECHA has replied to your comment under request C.1.

3. Long-term toxicity testing on aquatic invertebrates

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

You have adapted this 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. ECOSAR estimate on the Substance on Mysid shrimp
ii. ECOSAR estimate on the Substance on Daphnids
iii. Study performed on source substance 2-methylpropan-1-ol (EC 201-148-0) ([redacted] 1989)

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 211 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 reproduction 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 211 indicate that the percentage of mortality of the parent animals (female *Daphnia*) is ≤ 20% at the end of the test.

However, no information on the mortality of parent animals was provided.

Therefore, validity criteria is not fulfilled. Thus, the provided study cannot be considered a reliable source of information that could contribute to the conclusion on this key parameter investigated by the required study.

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

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.

In your comments to the draft decision you refer to Annex IX 9.1. Column 2 waiving possibilities. According to you *"the CSR/CSA registered for these substances does not indicate the need to further investigate the effects on aquatic organism. The results of the chemical safety assessment (CSA) show that all PEC/PNEC values are below the trigger value of 1, therefore, there is not relevant exposure of the substance to the aquatic environment."*

We have assessed this information and identified the following issue:

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

Therefore, your adaptation is rejected.

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 Section A.4.

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 adapted this the information requirement by using weight of evidence according to Annex XI, Section 1.2. ECHA understands that in support of your adaptation, you have provided the following sources of information:

i. ECOSAR estimate on the Substance on freshwater fish
ii. ECOSAR estimate on the Substance on saltwater fish
iii. OECD TG 210 on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) ([redacted] 1976)
iv. OECD TG 212 on source substance carbon disulphide (EC 200-843-6) (EPA/OTS, 1994)
v. OECD TG 210 on source substance sodium O-ethyl dithiocarbonate (EC 205-440-9) ([redacted] 1976)

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

We have assessed this information and identified the following issues:

To fulfil the information requirement, normally a study according to OECD TG 210 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 fish reproduction.

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 210 and 212 indicate that the overall survival of fertilised eggs in the controls is ≥ to the limits specified for the test species. Both test guidelines state that the analytical measure of the test concentrations must be conducted.

However, no analytical measurement of test concentrations and no information in the survival of fertilised eggs in any of the controls of all the studies were provided.

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.

In your comments to the draft decision you refer to Annex IX 9.1. Column 2 waiving possibilities. According to you *"the CSR/CSA registered for these substances does not indicate the need to further investigate the effects on aquatic organism. The results of the chemical safety assessment (CSA) show that all PEC/PNEC values are below the trigger value of 1, therefore, there is not relevant exposure of the substance to the aquatic environment."*

We have assessed this information and identified the following issue:

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

Your adaptation is rejected for the same reasons as developed under request C.3 above.

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 Section A.4.

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[10].

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[11].

[10] https://echa.europa.eu/practical-guides
[11] https://echa.europa.eu/manuals

Appendix E: 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 F: Procedure

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

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

The compliance check was initiated on 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 G: List of references - ECHA Guidance[12] 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)[13]

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]

[12] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[13] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[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 H: 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]
[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.