EUROPEAN CHEMICALS AGENCY

Helsinki, 11 June 2020

Addressees
Registrants of JS_S_ISOBUTYL_XANTHATE listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
14 September 2016

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Sodium O-isobutyl dithiocarbonate
EC number: 246-805-2
CAS number: 25306-75-6

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

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***16 September 2022***.

A. Requirements applicable to 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) with the Substance;
2. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method EU B.13/14. / OECD TG 471) with the Substance;
3. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method EU C.2./OECD TG 202) with the Substance;
4. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method EU C.3./OECD TG 201) with the Substance;

B. Requirements applicable to 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) with the Substance;
2. Only if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained, In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method OECD TG 476 or TG 490) with the Substance;
3. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method OECD TG 203) with the Substance;

C. Requirements applicable to all the Registrants subject to Annex IX of REACH

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method OECD TG 408) in rats with the Substance;
2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method OECD TG 414) in a first species (rat or rabbit), oral route with the Substance;
3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test

method EU C.20./OECD TG 211) with the Substance;

4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method OECD TG 210) with the Substance;

D. Requirements applicable to all the Registrants subject to Annex X of REACH

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method OECD TG 414) in a second species (rabbit or rat), oral route with the Substance.

Conditions to comply with the requests

Each addressee of this decision is bound by the requests for information corresponding to the REACH Annexes applicable to their own registered tonnage of the Substance at the time of evaluation of the jointly submitted dossier.

To identify your legal obligations, please refer to the following:

- you have to comply with the requirements of Annexes VII, VIII and IX of REACH, if you have registered a substance at 100-1000 tpa;
- you have to comply with the requirements of Annexes VII to X of REACH, if you have registered a substance at above 1000 tpa.

Registrants are only required to share the costs of information that they must submit to fulfil the information requirements for their registration.

The Appendix on general considerations addresses issues relevant for several requests while the other Appendices state the reasons for the requests for information to fulfil the requirements set out in the respective Annexes of REACH.

The Appendix entitled Observations and technical guidance addresses the generic approach for the selection and reporting of the test material used to perform the required studies and provides generic recommendations and references to ECHA guidance and other reference documents.

You must submit the information requested in this decision by the deadline indicated above in an updated registration dossier and also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information. The timeline has been set to allow for sequential testing where relevant.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Approved[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 general considerations

(i) Assessment of the weight-of-evidence adaptations, under the requirements of Annex XI, Section 1.2.

You have adapted the following standard information requirements by applying weight-of-evidence (WoE) approaches:

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX and X, Section 8.7.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.)

Your WoE adaptations are based on information on the Substance and/or similar substance(s), which you consider a group of xanthates, obtained through the use of data from the QSAR models and/or directly from information on similar substances from the public literature. The individual study records are mentioned under the relevant endpoints in the following Appendices to this decision.

We have assessed this information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation and identified the following general issues with all of these adaptations:

1. Requirement for documentation of the WoE adaptations

Annex XI, Section 1.2 states that there may be sufficient weight of evidence (WoE) 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. ECHA Guidance R.4.4 specifies that a WoE adaptation must involve an assessment of the relative values / weights of the several pieces of available information. This assessment must consider for instance the relevance and reliability of the information, the consistency of results/data, the nature and severity of effects. The lines of evidence should be integrated considering their relative values or weights in order to draw a conclusion. The assessment should be documented and included in your technical dossier.

However, you have not included a justification for your WoE adaptations, which would include an assessment of relative weights of the individual pieces of information and the subsequent conclusions drawn.

2. Reliability of the experimental information

ECHA Guidance R.4, Section R.4.2 informs on the criteria for assessing the reliability of information provided as part of WoE adaptations. The availability of raw data from the studies and an adequate description of the studies are listed among the key elements to be assessed to determine if and how the information can be used in the adaptation. This ECHA Guidance indicates that "*where critical supporting information is not reported (e.g. species tested, substance identity and dose procedure) the test data should be considered to be unreliable for the purposes of REACH*".

None of the study summaries provided by you, performed either on the Substance or an analogue substance, include any critical supporting information such as study design details, a description of the test solution preparation or other key parameters allowing to assess the validity of the test method applied. In the absence of this information the results of these studies referred to in your WoE adaptations are considered unreliable.

In the comments on the draft decision, you indicate an intention to acquire the "primary data" referred to in the dossier. In the absence of reliable primary data, you intend to perform new studies without specifying the studies nor the substance to be tested.

3. Relevance and reliability of the QSAR information

Whenever sources of information derived from QSAR predictions are used as part of a WoE, the following cumulative conditions shall be necessarily met: results are derived from a (Q)SAR model whose scientific validity has been established; the substance falls within the applicability domain of the model; results are adequate for the purpose of classification and labelling and/or risk assessment; adequate and reliable documentation of the applied method is provided.

According to ECHA's Practical guide "How to use and report (Q)SARs", section 3.4, 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.

For toxicological endpoints, you have provided QSAR model prediction reports detailing the structural and mechanistic criteria used for identifying the similar substances and providing high level information on the identity of these substances. We have assessed this information and conclude that the Substance does not fall within the applicability domain because the Substance has a dithiocarbonate functional group, which is not covered by the training set of the applied model either in its acidic or anionic form. Furthermore, the output also mentions that the fragment C(S)-O present in the Substance is similar to a known biophore C(S)-N, and therefore the Substance should be tested experimentally.

For ecotoxicological endpoints, you have provided QSAR predictions, however you have not provided QMRFs and QPRFs in your dossier. There is no adequate and reliable documentation for the QSAR predictions. Therefore the prediction from these QSAR models is considered as unreliable and irrelevant in the context of these WoE approaches.

4. Relevance of information – requirement for a scientific justification for the use of information from similar substances

Based on the ECHA Guidance R.4, Section R.4.3.2.2., a scientific justification needs to establish why the toxicological or ecotoxicological properties of the Substance can be determined from information on similar substances. It should also explain why the differences between these substances should not influence the toxicological/ecotoxicological properties of the Substance or should do so in a regular predictable pattern.

You have provided information on multiple similar substances. Details on the identity of these substances and on the nature of the information are provided in the endpoint sections in the next Appendices. In order to justify the use and relevance of this information to identify the properties of the Substance you have indicated in Part B Section 1.3 of your Chemical Safety Report (CSR) that the substances share structural similarities and decompose via physical and biological processes to common products: carbon disulfide, an alcohol and alkali

hydroxide. Your justification refers to the formation of common products via physical and biological processes. However you have not provided any qualitative and quantitative information characterising these processes to support your claim of formation of common products.

In the comments on the draft decision, you propose to perform a stability study under pH 1, 4, 7, and 9 with the Substance including an analysis of the metabolites to confirm the suspected degradation pathway. With this information you intend to improve the existing grouping for xanthates. You anticipate that this information will support your claim that "*hazardous properties can be largely predicted from understanding of biological and abiotic metabolites*".

In addition to the investigations on the hydrolysis of the Substance, you indicate that the biological degradation pathways will be examined. ECHA understands that you intend to use this information to confirm and characterise the formation of the metabolites from the Substance in order to establish the relevance of the information on these metabolites for the identification of the toxicological properties of the Substance.

However in your comments to the draft decision you do not provide detailed information on the exact nature of the investigations that you intend to perform.

It is not possible to confirm on the basis of the information provided whether these investigations may inform on the rate and extent of the formation of the common compound that you consider driving the toxicity of the substances.

It is unclear how you intend to address the potential exposure to the substances in their native form, i.e. as non-metabolised compounds. Whilst you re-iterate your intentions to predict the properties of the Substance using information from the common compound, you do not elaborate on the impact of exposure to non-common compounds formed from the substances on the relevance of the information obtained from the analogue substance.

Furthermore, the results of the stability investigations you have announced in your comments are not yet available and they may or may not confirm your hypothesis. While you intend to perform bacterial gene mutation and *Daphnia* immobilisation studies to validate the read-across, you do not explain the relevance of how this information would support the mutagenicity or higher tier vertebrate testing as requested in the present Decision in Appendices C and D.

Currently, you have not established why the toxicological properties of the Substance can be determined from information on these similar substances. Consequently, this information cannot be considered as relevant for the purpose of identification of the hazard of the Substance by means of weight of evidence.

With respect to the ecotoxicological endpoints, the shortcomings of your read-across and the proposed plans of further investigations are discussed in section iii of the present Appendix. These findings apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptations.

Conclusion of the WoE assessment

For the reasons presented above, as your WoE adaptations are neither based on data which allow a conclusion on the relevant hazard properties of the Substance nor supported by adequate documentation, they do not comply with the general rules of adaptation as set out in Annex XI, Section 1.2. Therefore, your adaptations are rejected.

(ii) Assessment of the QSAR adaptations, under the requirements of Annex XI, Section 1.3.

You have adapted the following standard information requirements by applying QSAR approach in accordance with Annex XI, Section 1.3:

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

We have assessed this information and identified the following general issues:

For the use of QSAR models under Annex XI, Section 1.3., the following cumulative conditions shall be necessarily met: results are derived from a (Q)SAR model whose scientific validity has been established; the substance falls within the applicability domain of the model; results are adequate for the purpose of classification and labelling and/or risk assessment; adequate and reliable documentation of the applied method is provided.

According to ECHA's Practical guide "How to use and report (Q)SARs", section 3.4, 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.

However, the information you have provided does not meet the cumulative conditions mentioned above. The Substance does not fall within the applicability domain of the model (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) because the Substance has a dithiocarbonate functional group, which is not covered by the training set of the applied model either in its acidic or anionic form (see also Section (i).3 above). Therefore, the results are inadequate for classification and labelling and/or risk assessment.

Although documentation was provided for toxicological endpoints, you have not provided any documentation for the QSAR predictions on the environmental endpoint (in particular, you have not included a QMRF and a QPRF in your technical dossier).

For the reasons presented above, your QSAR adaptations are rejected.

(iii) Assessment of the Grouping of substances and read-across approach, under the requirements of Annex XI, Section 1.5.

You have adapted the following standard information requirements by applying read-across approaches in accordance with Annex XI, Section 1.5:

- Surface tension (Annex VII, Section 7.6.)
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

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

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. Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6 and the ECHA RAAF document.

You read-across between the structurally similar substances, sodium O-ethyl dithiocarbonate, EC No. 205-440-9 (CAS No. 140-90-9) as source substance and the Substance as target substance.

You indicate that these substances belong to a group of "xanthates". According to the information provided in your Chemical Safety Report, *"The group of the compounds is called xanthates, derived from the xanthate radical:* [redacted] *They are products of a reaction between carbon disulfide, relevant alcohol and sodium or potassium hydroxide. Each of the substances: contain common functional group –* [redacted] *decomposes via physical and biological processes to common products: carbon disulfide, an alcohol and alkali hydroxide, is characterized by a constant pattern in the changing of the properties across the category."*

In the comments on the draft decision, you further clarified your hypothesis and noted that "*hazardous properties can be largely predicted from understanding of biological and abiotic metabolites*". ECHA understands from this information that you intend to predict the properties of the Substance using a read-across which is based on the formation of common (bio)transformation products.

1. Missing information on the composition of the source substances regarding the Surface tension endpoint

Annex XI, Section 1.5 of the REACH Regulation provides that "*substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of chemical similarity may be considered as group.*"

According to the ECHA Guidance, "*the purity and impurity profiles of the substance and the structural analogue need to be assessed*". The purity profile and composition can influence the overall properties of the Substance and of the source substance(s).[2] Therefore, qualitative and quantitative information on the compositions of the Substance and of the source substance(s) should be provided to allow assessment whether the attempted predictions are compromised by the composition and/or impurities.

In your technical dossier you have described the source substance(s) only by its name, EC and CAS numbers. No information on the composition of this substance is reported.

Without detailed information on the composition of the source substance(s), no qualitative or quantitative comparative assessment of the compositions of the Substance and of the source substance(s) can be completed. Therefore, ECHA considers that it is not possible to assess whether the attempted predictions are compromised by the composition of the source substance(s).

[2] ECHA Guidance R.6 R.6: Section R.6.2.3.1

In your comments to the draft decision, you agreed that the read-across adaptation is not acceptable.

2. Missing supporting information regarding Long-term toxicity testing on aquatic invertebrates

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*"[3]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Missing information on the formation of common compound

As your hypothesis is based on the formation of common (bio)transformation products, information characterising the rate and extent of the (bio)transformation of the Substance and of the source substance(s) is necessary to confirm the formation of the proposed common (bio)transformation product and to assess the impact of the exposure to the parent compounds.

In your comments you state that you intend to perform a stability study under pH 1, 4, 7, and 9 with analysis on metabolites to confirm the suspected degradation pathway.

The registration dossier also includes hydrolysis data with reported half-life of 260hr in pH 7. This existing data indicates that in fact the hydrolysis of the Substance in aqueous solution may not be fast and this contradicts your presented hypothesis. However, this hydrolysis data has the same deficiencies in reporting as described above in section (i).2 above and cannot be considered reliable.

You have not provided experimental data or other adequate and reliable information for the hydrolysis of the source substance.

In the absence of reliable information characterising the rate and extent of transformation of the Substance and of the source substance(s), you have not provided sufficient supporting information to strengthen the rationale for the read-across.

Missing information on the impact of non-common compounds

As your hypothesis is based on the formation of common (bio)transformation products, the impact of exposure to non-common compounds, such as the parent compounds and non-common degradation products, needs to be assessed to ensure that a reliable prediction can be made for the endpoint in question (e.g. effects on the reproductive output of *Daphnia magna* for endpoint Long-term toxicity testing on aquatic invertebrates).

You indicate that degradation of the Substance and other substances in the xanthates group form the common compound carbon disulfide, and non-common compounds such as an alcohol and alkali hydroxide.

[3] ECHA Guidance R.6, Section R.6.2.2.1.f

You have not explained nor provided evidence for the impact of exposure to these non-common compounds and the parent substances on the properties of the Substance.

In the comments on the draft decision you indicate that you intend to perform *Daphnia* immobilisation study to "validate the read-across". You do not further explain on which substances you intend to perform this test, nor you further explain in which way such information may support your hypothesis for this endpoint. ECHA notes that *Daphnia* immobilisation studies do not inform on the effects on the reproductive output of *Daphnia magna,* which is investigated in a study according to OECD TG 211.

In the absence of information addressing the impact of exposure to the non-common compounds, you have not established that a reliable prediction of the property under consideration of the Substance can be derived on the basis of your read-across hypothesis. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

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 analogue substances. Therefore, your adaptations do not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approaches are rejected.

Appendix A: Reasons for the requests to comply with Annex VII of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 1 to 10 tonnes or more per year must contain, as a minimum, the information specified in Annex VII to REACH.

1. Surface tension (Annex VII, Section 7.6.)

Surface tension is a standard information requirement in Annex VII to REACH.

You have provided the following information for this endpoint:

i. An adaptation: "*This endpoint is waived in accordance with Column 2 of Annex VII of the REACH Regulation as the substance is a solid at room temperature; the endpoint is not relevant.*"
ii. Supporting study according to OECD TG 115 and GLP with the analogue substance sodium O-ethyl dithiocarbonate (EC 205-440-9).
iii. Supporting study according to EU A.5 and GLP with the Substance.

ECHA has evaluated this information and identified the following deficiencies:

i. According to Annex VII, Section 7.6, Column 2, the study need only be conducted if, a) based on structure, surface activity is expected or can be predicted, or b) surface activity is a desired property of the material.

   ECHA cannot relate your adaptation statement (substance is solid at room temperature) to any of these two scenarios and therefore considers that it is not a valid 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.

   In your comments to the draft decision, you agreed that the adaptation is not acceptable.

ii. As explained in the Appendix on general considerations (iii), your adaptation using study (ii) is rejected.

   In your comments to the draft decision, you agreed that the read-across adaptation is not acceptable.

iii. In order to be compliant for this endpoint, a study must be performed according to EU A.5 or OECD TG 115 guidelines which specify that the test concentration should be 90% of the saturation solubility, but, when this concentration exceeds 1 g/l, a concentration of 1 g/l is used in the test.

   The water solubility reported in the dossier is 510 g/l at 20 °C. A 90 % solution of the Substance equals approximately 459 g/l, i.e. it exceeds 1 g/l, and therefore, the test concentration for the Substance must be 1 g/l. The test concentration reported in study iii) is 37 %, equalling approximately in 189 g/l test concentration. This concentration is significantly higher than 1 g/l. Therefore, the study was not performed according to the test guideline, and is rejected.

   In your comments to the draft decision you indicated that the study has been conducted in accordance with the guideline, but it has been wrongly reported in the dossier. You note that the full study report attached to your dossier reports an experimentally measured value for a 1 g/l water solution (64.9 mN/m at 20 °C). In your comments you committed to update the dossier and CSR to reflect the correct information i.e. the information measured for the 1 g/l solution. ECHA agrees that the

study was performed according to OECD TG 115 and GLP, but the necessary corrections are not yet in the dossier.

Based on the deficiencies listed above, the information requirement is not yet fulfilled.

2. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)

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

You have adapted the standard information requirement according to Annex XI, Section 1.2. weight-of-evidence of REACH. In support of this adaptation of the information requirement, you have provided the following information for this endpoint:

i. With analogue substance carbon disulphide (CAS: 75-15-0, EC: 200-843-6), U.S. Department of Health and Human Services, 1996 - *in vitro* gene mutation study in bacteria, similar to OECD Test Guideline 471;

ii. Information obtained from QSAR prediction (2012) on the Substance, A7A-A7E from FDA Genetic toxicity set. Model: MC4PC version 2.4.1.5c.

We have assessed this information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation and identified the following issue(s):

As explained in the Appendix on general considerations (i) (1, 2, 3, 4) your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

3. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)

Short-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex VII to REACH.

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH. In support of this adaptation of the information requirement, you have provided the following information for this endpoint:

i. a key study (1988) on analogue substance (sodium ethyl xanthate; CAS: 140-90-9, EC: 205-440-9), performed according to OECD TG 202;

ii. a study (1977) on the Substance, performed according to OECD TG 202;

iii. 2 studies (1979 and 1995) on analogue substance (sodium ethyl xanthate), first performed according to OECD TG 202 and second with not specified test method).

We have assessed this information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation and identified the following issue(s):

As explained in the Appendix on general considerations (i) (1, 2, 4) your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

4. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

Growth inhibition study aquatic plants is a standard information requirement in Annex VII to REACH.

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH. In support of this adaptation of the information requirement, you have provided the following information for this endpoint:

i. a key study on algae (2000) on the Substance, performed according to the method: Reduction of chlorophyll concentration/ Algae (Monoraphidium griffithii) growth rate test;

ii. a key study on plants other than algae (2000) on the Substance, performed according to OECD TG 221;

iii. a study on algae (1977) on the Substance, performed according to OECD TG 201;

iv. 3 studies (1979, 1979 and 1995) on analogue substance (sodium ethyl xanthate):
   - First, test on algae, performed according to OECD TG 201,
   - Second, test on plants other than algae, performed according to OECD TG 221,
   - and for a third one, test on algae, you have not specified a test method.

v. a study (1988) on analogue substance (sodium isopropyl xanthate CAS: 140-93-2, EC: 205-443-5), performed according to OECD TG 221.

We have assessed this information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation and identified the following issue(s):

As explained in the Appendix on general considerations (i) (1, 2, 4) your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

Appendix B: Reasons for the requests to comply with Annex VIII of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 10 to 100 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII and VIII to REACH.

1. In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)

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 the standard information requirement according to Annex XI, Section 1.2. Weight of evidence of REACH.

In support of this adaptation of the information requirement, you have provided the following information for this endpoint:

i. Information obtained from QSAR prediction on the Substance, *in vitro* cytogenicity / chromosome aberration study (2012) on the Substance, A7U-A7X and A8H from FDA Genetic toxicity set. Model version: MC4PC version 2.4.1.5;

ii. Information obtained from QSAR prediction on the Substance, genetic toxicity *in vitro*.ToxTree: Benigni/Bossa rules for carcinogenicity and mutagenicity.

We have assessed this information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation and identified the following issue(s):

As explained in the Appendix on general considerations section (i) (1, 3) your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

2. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

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.

You have adapted the standard information requirement according to Annex XI, Section 1.3. QSAR of REACH.

In support of this adaptation of the information requirement, you have provided the following information for this endpoint:

i. Information obtained from QSAR prediction on the Substance, *in vitro* gene mutation study in mammalian cells, Model name: A7O, A7N, AN7 and AN8 from FDA Genetic toxicity set Model version: MC4PC version 2.4.1.5.

We have assessed this information according to the requirements of Annex XI, Section 1.3 of the REACH Regulation and identified the following issue(s):

As explained in the Appendix on general considerations section (ii) your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

3. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

Short-term toxicity testing on fish is a standard information requirement in Annex VIII to REACH.

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH. In support of this adaptation of the information requirement, you have provided the following information for this endpoint:

i. 5 key studies (1976, 1986) on the Substance, performed according to OECD TG 203;

ii. 3 studies (1977) on the Substance, performed according to OECD TG 203;

iii. 4 studies (1977) on analogue substance (sodium ethyl xanthate) performed according to EPA OTS 797, 1400;

iv. 5 studies (1995) on analogue substance (Potassium amyl xanthate, EC:2720-73-2, CAS: 220-329-5), performed according to OECD TG 203;

v. 5 studies (1976) on analogue substance (Potassium ethyl xanthate, EC:140-89-2):

- 1st to 4th performed according to OECD TG 203
- and for the fifth one you have not specified a test method;

vi. a study (2000) on analogue substance (Potassium isobutyl xanthate, EC:13001-46-2, CAS: 235-837-2), performed according to OECD TG 203;

vii. 3 studies (1973) on analogue substance (Sodium isopropyl xanthate, EC:140-93-2, CAS: 205-443-5), performed according to OECD TG 203;

We have assessed this information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation and identified the following issue(s):

As explained in the Appendix on general considerations (i) (1, 2, 4) your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

Appendix C: Reasons for the requests to comply with Annex IX of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 100 to 1000 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII to IX to REACH.

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

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

You have adapted the standard information requirement according to Annex XI, Section 1.2. Weight of evidence of REACH.

In support of this adaptation of the information requirement, you provided the following information from analogue substance for this endpoint, three oral studies and seven inhalation studies:

i. Australian Government Publishing Service Canberra, 1995, Potassium butyl xanthate (CAS No: 871-58-9 EC No: 212-808-2), similar to OECD TG 408 (Repeated Dose 90-Day Oral Toxicity in rats);
ii. Canadian Centre for Occupational Health and Safety Year, 2010, Potassium ethyl xanthate (CAS No: 140-89-6 EC No: 205-439-3), no guideline mentioned;
iii. U.S. Department of Health and Human Services Year 1996, Carbon disulfide (CAS No: 75-15-0 EC No: 200-843-6) similar to OECD TG 407 (Repeated Dose 28-Day oral Toxicity in rats);
iv. Australian Government Publishing Service Canberra, 1995, Potassium amyl xanthate (CAS No: 2720-73-2 EC No: 220-329-5), similar to OECD TG 412 (Subacute Inhalation Toxicity: 28-Day Study in mice);
v. Australian Government Publishing Service Canberra, 1995, Potassium amyl xanthate (CAS No: 2720-73-2 CAS No: 220-329-5), similar to OECD TG 412 (Subacute Inhalation Toxicity: 28-Day Study in rats);
vi. Australian Government Publishing Service Canberra, 1995, Potassium amyl xanthate (CAS No: 2720-73-2 EC No: 220-329-5), similar to OECD TG 412 (Subacute Inhalation Toxicity: 28-Day Study in rabbits);
vii. Australian Government Publishing Service Canberra, 1995, Potassium amyl xanthate (CAS No: 2720-73-2 EC No: 220-329-5), similar to OECD TG 412 (Subacute Inhalation Toxicity: 28-Day Study in dogs);
viii. U.S. Department of Health and Human Services Year 1996, Carbon disulphide (CAS No: 75-15-0 EC No: 200-843-6), no guideline mentioned;
ix. U.S. Department of Health and Human Services Year 1996, Carbon disulphide (CAS No: 75-15-0 EC No: 200-843-6), similar to OECD TG 413 (Subchronic Inhalation Toxicity: 90-Day Study in rats);
x. U.S. Department of Health and Human Services Year 1996, Carbon disulphide (CAS No: 75-15-0 EC No: 200-843-6), similar to OECD TG 413 (Subchronic Inhalation Toxicity: 90-Day Study in mice).

We have assessed this information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation and identified the following issue(s):

As explained in the Appendix on general considerations (i) (1, 2, 4), your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the Substance is a solid and is used as such with low dustiness. The use information provided in the Chemical Safety Report indicates that human exposure to the Substance by the inhalation route is unlikely.

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

In your comments you noted that the vertebrate testing would need to be performed in a tiered approach, with "*subchronic toxicity helping to set dose levels for any reproductive toxicity testing*". ECHA confirms that the timeline has been already set up to allow for such sequential testing.

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first 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 the standard information requirement according to Annex XI, Section 1.2 (Weight of evidence).

In support of this adaptation of the information requirement, you provided the following information from analogue substance for this endpoint,

i. U.S. Department of Health and Human Services Year 1996, Carbon disulphide (CAS No: 75-15-0 EC No: 200-843-6), similar to OECD TG 414 (Prenatal Developmental Toxicity Study) inhalation, rabbit;
ii. U.S. Department of Health and Human Services Year 1996, Carbon disulphide (CAS No: 75-15-0 EC No: 200-843-6) similar to OECD TG 414 (Prenatal Developmental Toxicity Study) oral, rat;
iii. U.S. Department of Health and Human Services Year 1996, Carbon disulphide (CAS No: 75-15-0 EC No: 200-843-6) similar to OECD TG 414 (Prenatal Developmental Toxicity Study) inhalation, rat;
iv. U.S. Department of Health and Human Services Year 1996, Carbon disulphide (CAS No: 75-15-0 EC No: 200-843-6) similar to OECD TG 414 (Prenatal Developmental Toxicity Study) inhalation, mouse.

We have assessed this information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation and identified the following issue(s):

As explained in the Appendix on general considerations (i) (1, 2, 4), your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

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

In your comments you noted that the vertebrate testing would need to be performed in a tiered approach, with "*subchronic toxicity helping to set dose levels for any reproductive toxicity testing*". ECHA confirms that the timeline has been already set up to allow for such sequential testing.

3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section

9.1.5.)

Long-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex IX to REACH.

You have provided:

i. a key study (2013) on analogue substance (sodium ethyl xanthate; CAS: 140-90-9, EC: 205-440-9), performed according to OECD TG 211.

ECHA thus considers that you submitted an adaption of the standard information requirement by using a read-across approach under Annex XI, Section 1.5.

However, as explained in the Appendix on general considerations section (iii), your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

Long-term toxicity testing on fish is a standard information requirement in Annex IX to REACH.

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH. In support of your adaptation of this information requirement, you have provided the following information for this endpoint:

i. 2 studies (1995) on analogue substance (sodium ethyl xanthate), performed according to OECD TG 215;
ii. 2 studies (Leduc G. et all, 1976 and Webb M. et all, 1976) on analogue substance (potassium O-pentyl dithiocarbonate, CAS: 2720-73-2, EC: 220-329-5) performed according to OECD TG 210;
iii. 2 QSAR predictions (EPA ECOSAR 1.1) for the Substance.

We have assessed this information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation and identified the following issue(s):

As explained in the Appendix on general considerations (i) (1, 2, 3, 4), your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

Appendix D: Reasons for the requests to comply with Annex X of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier at a tonnage above 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to REACH.

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species

Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is a standard information requirement under Annex X to REACH.

You have adapted the standard information requirement according to Annex XI, Section 1.2 (Weight of Evidence), providing the information mentioned in Appendix C, Section 2 above.

We have assessed the information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation, as described in Appendix C, Section 2.

As explained in the Appendix on general considerations (i) (1, 2, 3, 4) your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

A PNDT study according to the OECD TG 414 study should be performed in rabbit or rat as the preferred second species, depending on the species tested in the first PNDT study (request C.2. in this decision) with oral administration of the Substance.

In your comments you noted that the vertebrate testing would need to be performed in a tiered approach, with "*subchronic toxicity helping to set dose levels for any reproductive toxicity testing*". ECHA confirms that the timeline has been already set up to allow for such sequential testing.

Appendix E: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of registration dossiers after the date on which you were notified the draft decision according to Article 50(1) of REACH.

The compliance check was initiated on 14 March 2019.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision and invited you to provide comments within 30 days of the notification.

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

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

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

Appendix F: Observations and technical guidance

1. The information requirement under Section 8.7.3. of Annex IX/X to REACH (Extended one-generation reproductive toxicity study, EOGRTS) is not addressed in this decision, because the information from the Sub-chronic toxicity study (90-day), requested in the present this decision, is relevant for the study design of the EOGRTS.

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

3. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of the Member States.

4. Test guidelines, GLP requirements and reporting

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

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

   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: 'How to report robust study summaries'[4].

5. Test material

   Selection of the test material(s)

   The registrants of the Substance are responsible for agreeing on the composition of the test material to be selected for carrying out the tests required by the present decision. The test material selected must be relevant for all the registrants of the Substance, i.e. it takes into account the variation in compositions reported by all members of the joint submission. The composition of the test material(s) must fall within the boundary composition(s) of the Substance.

   While selecting the test material you must take into account 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.

   Technical reporting of the test material

   The composition of the selected test material must be reported in the respective endpoint study record, under the Test material section. The composition must include all constituents of the test material and their concentration values [and other parameters relevant for the property to be tested, in this case...]. Without such detailed

[4] https://echa.europa.eu/practical-guides

reporting, ECHA may not be able to confirm that the test material is relevant for the Substance and to all the registrants of the Substance.

Technical instructions are available in the manual "How to prepare registration and PPORD dossiers"[5].

6. List of references of the ECHA Guidance and other guidance/ reference documents[6]

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 in this decision.

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 in this decision.

ECHA Read-across assessment framework (RAAF, March 2017)[7]

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.

OECD Guidance documents[8]

[5] https://echa.europa.eu/manuals
[6] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[7] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[8] 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 GD23.
Guidance Document on Mammalian Reproductive Toxicity Testing and Assessment – No 43, referred to as OECD GD43.

Appendix G: List of the registrants to which the decision is addressed and the corresponding information requirements applicable to them

Registrant Name	Registration number	(Highest) Data requirements to be fufilled
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Note: where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas the decision is sent to the actual registrant.