~~Confidential~~

Helsinki, 10 November 2021

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

Date of submission of the dossier subject to this decision
02/09/2016

Registered substance subject to this decision ("the Substance")
Substance name: Sodium O-ethyl dithiocarbonate
EC number: 205-440-9
CAS number: 140-90-9

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

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

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

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

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

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

3. 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. 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 fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

D. Information required from 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) by oral route, in a second species (rat or rabbit)

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 X 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 Annex VII to REACH, for registration at 1-10 tpa, or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

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

How to comply with your information requirements

To comply with your information requirements you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

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

Appeal

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

Failure to comply

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

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

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

Appendix on Reasons common to several requests

1. **Assessment of your weight of evidence adaptation under 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.)
- In vitro mammalian cell gene mutation study (Annex VIII, Section 8.4.3.)
- 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.

ECHA 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.

3. Reliability of the QSAR information

Whenever sources of information derived from QSAR predictions are used as part of a WoE, the cumulative conditions outlined under section 2 Assessment of your QSAR adaptations under Annex XI, Section 1.3. of this Appendix shall be necessarily met. As explained under the section 2 of this Appendix, the predictions based the provided QSAR information are not considered reliable. Therefore the information cannot be used in support of the WoE approaches.

4. Reliability 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.,[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 reliability 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 absence of such information 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 reliable for the purpose of identification of the hazard of the Substance by means of weight of evidence.

Additional elements of the weight of evidence adaptations are addressed in the corresponding Appendices.

2. Assessment of your QSAR adaptations under 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.)
- In vitro mammalian cell gene mutation study (Annex VIII, Section 8.4.3.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

[2] See also ECA Guidance R.6, Section R.6.2.2.1.f.

ECHA 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.

A. 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.

   You have not provided the required documentation for the QSAR prediction on the long-term toxicity testing on fish endpoint (in particular, you have not included a QPRF in your technical dossier).

   ECHA also notes lack of documentation of the model (QMRF and QPRF missing) for the BeningniBossa rulebase in ToxPredict (QSAR prediction for carcinogenicity and mutagenicity) and Lazar Structure- Activity Relationships. The information was not considered further in absence of documentation.

B. The substance must fall within the applicability domain of the model.

   For ecotoxicological endpoint, you have applied the ECOSAR model (version 1.10) to make a prediction for the Substance and the source substance sodium O-isobutyl dithiocarbonate (EC 246-805-2).

   The Substance and the source substance have a dithiocarbonate functional group. However, based on the publicly available information on the applied ECOSAR model (Version 1.10), this functional group is not covered by its training set.

   In addition, you do not explain how the result of the test material substances is related to the registered substance

   For toxicological endpoints, the Substance does not fall within the applicability domain of the model as defined by model developer or automatically indicated by the applied modeller software.

   Therefore, you have not demonstrated that your QSARs meet the above condition.

C. Under ECHA Guidance R.6.1.3., a (Q)SAR model must fulfil the principles described in the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) to be considered scientifically valid. The first OECD principle requires the endpoint of a (Q)SAR model to be well defined. ECHA Guidance R.6.1.5.2 specifies that for a well-defined endpoint the effect modelled being predicted by the (Q)SAR must be the same as the effect measured by a defined test protocol relevant to the information requirement.

   For mutagenicity, you have provided a prediction using the MultiCase for bacterial reverse mutation test, MultiCase in vitro Mammalian chromosome aberration test, and MultiCase in vitro Mammalian cell gene mutation test QSAR.

   The predicted toxicological effects are not the same as the effects measured by the

required corresponding guideline test methods (OECD TG 471, 473, 487 and 476) because the information is converted and provided in MCASE units that do not correspond to regulatory endpoints, respectively.

Therefore, you have not demonstrated that these QSARs meet the above condition.

For the reasons presented above, the provided information is not adequate for the purpose of classification and labelling and/or risk assessment, and your QSAR adaptations are rejected.

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.

You have provided the following information:

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. Key study according to OECD TG 115 and GLP with the registered substance sodium O-ethyl dithiocarbonate (EC 205-440-9).

ECHA has evaluated this information and identified the following deficiencies:

i. You have adapted the information under Annex VII, Section 7.6., Column 2.
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.

   Therefore, the adaptation is rejected.

ii. Key study according to OECD TG 115

   The OECD TG 115 specifies that the test concentration is 90% of the saturation solubility in water, but when this concentration exceeds 1 g/l, a concentration of 1 g/l is used in the test.

   You have provided a study performed with a test concentration of 36% by weight. The test concentration is above the maximum concentration of 1 g/l, and therefore, the results cannot be considered reliable for chemical safety assessment.

   The provided study does not fulfil the requirements of the OECD TG 115 and is rejected.

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

2. In vitro gene mutation study in bacteria

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

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

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

i. *in vitro* gene mutation study in bacteria (1996) with source substance carbon disulphide (CAS 75-15-0, EC 200-843-6)
ii. QSAR prediction (2012) on the Substance, model name A7A-A7E from FDA Genetic toxicity set (MC4PC version 2.4.1.5)

iii. QSAR predictions on the Substance without specifying the predicted information requirement (ToxTree: Benigni/Bossa rules for carcinogenicity and mutagenicity, and Lazar Structure- Activity Relationships).

ECHA 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 Reasons common to several requests section 1, 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.

To fulfil the information requirement, normally a study according to OECD TG 471 must be provided. The key investigations of this test are:

- Detection and quantification of gene mutations (base pairs, substitution or frame shift) in cultured bacteria including data on the number of revertant colonies; and
- Data provided on 5 bacterial 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 source of information i.) you provided investigates strain T98. Therefore, it provides partially relevant information that would contribute to the conclusion on the key investigations. However, the study summary provided by you on the source of information i) is very limited and does not allow ECHA to assess the validity or relevance of the test any further.

In addition, the reliability of these sources of information is significantly affected by the deficiencies identified in section 1 of the Appendix on Reasons common to several requests.

Taken together, the sources of information provide only partial information on the key investigations. In addition, 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 requirements are not fulfilled.

Study design

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

3. Short-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is a standard information requirement under 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 the Substance, performed according to OECD TG 202;
ii. 2 studies (1979 and 1995) on the Substance, 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 Reasons common to several requests sections 1, 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.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.2 at Annex VII includes similar information that is produced by the OECD TG 202. Therefore the following requirements must be met:

- the concentrations of the test material leading to the immobilisation of 50% of daphnids at the end of the test is estimated;

All the sources of information you provided are described as investigating the key investigations. However, the study summaries provided by you on the sources of information are very limited and does not allow ECHA to assess the validity or relevance of the test any further.

In addition, the reliability of these sources of information is significantly affected by the deficiencies identified in section 1 of the Appendix on Reasons common to several requests.

Taken together, none of the sources of information provide information on the key investigations. In addition, 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 one source of information alone 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 requirements are not fulfilled.

Therefore, the information requirement is not fulfilled.

4. Growth inhibition study aquatic plants

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 (1977) on the Substance, performed according to OECD TG 201;
ii. a key study on algae (2000) on analogue substance (sodium isobutyl xanthate), performed according to the method: Reduction of chlorophyll concentration/ Algae (Monoraphidium griffithii) growth rate test;
iii. a supporting study "CESARS - Chemical Evaluation Search and Retrieval System, AQUIRE - Aquatic Information Retrieval Computerized database, developed by U.S, EPA" on the Substance;
iv. a supporting study on algae (1985) on analogue substance (Carbon disulfide), performed according to OECD TG 201;

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 Reasons common to several requests section 1, 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.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.2 at Annex VII includes similar information that is produced by the OECD TG 201. Therefore the following requirements must be met:

- the concentrations of the test material leading to a 50% and 0% (or 10%) inhibition of growth at the end of the test are estimated.

All the sources of information you provided are described as investigating the key investigations. However, the study summaries provided by you on the sources of information are very limited and does not allow ECHA to assess the validity or relevance of the test any further.

In addition, the reliability of these sources of information is significantly affected by the deficiencies identified in section 1 of the Appendix on Reasons common to several requests.

Taken together, none of the sources of information provide information on the key investigations. In addition, 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 one source of information alone 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 requirements are not fulfilled.

Therefore, the information requirement is not fulfilled.

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

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

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

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

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

i. QSAR prediction (2012) on the Substance, model name A7U-A7X and A8H from FDA Genetic toxicity set (MC4PC version 2.4.1.5)

ECHA has 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 Reasons common to several requests section 1, the weight of evidence must fulfill the information requirement based on relevant and reliable sources of information. While information from a single source alone is not sufficient to support this notion and this would be a reason sufficient to reject the adaptation, these sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.2. at Annex VIII includes:

- 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 source of information you provided does not investigate these key investigations. Therefore, it does not provide relevant information that would contribute to the conclusion on these key investigations.

In addition, the reliability of these sources of information is significantly affected by the deficiencies identified in section 1 of the Appendix on Reasons common to several requests.

Taken together, none of the sources of information provide information on the key investigations. In addition, 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 one source of information alone 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 requirements are not fulfilled.

Study design

To fulfil the information requirement for the Substance, either *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

2. In vitro gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

Data in dossier: 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.

ECHA assessment: 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 sections 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.

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

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

i. QSAR prediction (2012) on the Substance, model name: A7O, A7N, AN7 and AN8 from FDA Genetic toxicity set (MC4PC version 2.4.1.5)

ECHA 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 Reasons common to several requests section 1, the weight of evidence must fulfill the information requirement based on relevant and reliable sources of information. While information from a single source alone is not sufficient to support this notion and this would be a reason sufficient to reject the adaptation, these sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.3 at Annex VIII includes similar information that is produced by the OECD TG 476/490 and OECD TG 488. This includes:

- 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 source of information you provided does not investigate these key investigations. Therefore, it does not provide relevant information that would contribute to the conclusion on these key investigations.

In addition, the reliability of these sources of information is significantly affected by the deficiencies identified in section 1 of the Appendix on Reasons common to several requests.

Taken together, the source of information does not provide information on the key investigations. In addition, its 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 one source of information alone 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 requirements are not fulfilled.

Consequently, you are required to provide information for this endpoint, if the *in vitro* gene mutation study in bacteria and the *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study provide a negative result.

Study design

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

3. 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 provided an adaptation according to Annex XI, Section 1.2. in your dossier.

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. 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);
ii. 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);
iii. 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);
iv. 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);
v. 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);

ECHA 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 Reasons common to several requests section 1, 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.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.6.1 at Annex VIII includes, at general level, information on systemic toxicity in intact, non-pregnant and young adult males and females from: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity. Information should address effects on the following physiological systems: circulatory system, digestive/excretory system, endocrine system, immune system, integumentary system, musculoskeletal system, nervous system, renal/urinary system, reproductive system, and respiratory system.

All the sources of information you provided are described as investigating the key

investigations. However, the study summaries provided by you on the sources of information are very limited and does not allow ECHA to assess the validity or relevance of the test any further.

In addition, the reliability of these sources of information is significantly affected by the deficiencies identified in section 1 of the Appendix on Reasons common to several requests.

Taken together, none of the sources of information provide information on the key investigations. In addition, 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 requirements are 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 1 of Appendix C). 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.

2. Short-term toxicity testing on fish

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. 4 key studies (1973, 1977) on the Substance, performed according to EPA OTS 797.1400 (Fish Acute Toxicity Test);
ii. 1 key study (1976) on the Substance, performed according to OECD TG 203;
iii. 5 studies (1995) on analogue substance (Potassium amyl xanthate, EC:2720-73-2, CAS: 220-329-5), performed according to OECD TG 203;
iv. 5 studies (1995) on analogue substance (Potasium ethyl xanthate) guideline not specified;
v. a study (2000) on analogue substance (Potassium isobutyl xanthate, EC:13001-46-2, CAS: 235-837-2), performed according to OECD TG 203;
vi. 4 studies (1973, 1976, 1986) on analogue substance (Sodium isobutyl xanthate, EC: 246-805-2, CAS: 25306-75-6), performed according to OECD TG 203;
vii. 3 studies (1973) on analogue substance (Sodium isopropyl xanthate, EC: 205-443-5, CAS: 140-93-2), 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 Reasons common to several requests section 1, 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.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.2 at Annex VII includes similar information that is produced by the OECD TG 203. Therefore the following requirements must be met:

- the concentration of the test material leading to the mortality of 50% of the juvenile fish at the end of the test is estimated.

All the sources of information you provided are described as investigating the key investigations. However, the study summaries provided by you on the sources of information are very limited and does not allow ECHA to assess the validity or relevance of the test any further.

In addition, the reliability of these sources of information is significantly affected by the deficiencies identified in section 1 of the Appendix on Reasons common to several requests.

Taken together, none of the sources of information provide information on the key investigations. In addition, 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 one source of information alone 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 requirements are not fulfilled.

Therefore, the information requirement is not fulfilled.

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 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. 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. 2010, Potassium ethyl xanthate (CAS No: 140-89-6 EC No: 205-439-3), no guideline mentioned;
iii. 1996, Carbon disulphide (CAS No: 75-15-0 EC No: 200-843-6), no guideline mentioned;
iv. 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);
v. 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).

ECHA 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 Reasons common to several requests section 1, 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.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.6.2 at Annex IX includes, at general level, information on systemic toxicity in intact, non-pregnant and young adult males and females from: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity. Information should address effects on the following physiological systems: circulatory system, digestive/excretory system, endocrine system, immune system, integumentary system, musculoskeletal system, nervous system, renal/urinary system, reproductive system, and respiratory system.

All the sources of information you provided are described as investigating the key investigations. However, the study summaries provided by you on the sources of information are very limited and does not allow ECHA to assess the validity or relevance of the test any further.

In addition, the reliability of these sources of information is significantly affected by the deficiencies identified in section 1 of the Appendix on Reasons common to several requests.

Taken together, none of the sources of information provide information on the key investigations. In addition, 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 requirements are not fulfilled.

Request for OECD TG 408 = oral route (dietary/gavage/drinking water)

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

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

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

i. 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. 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. 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. 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 Reasons common to several requests section 1, 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.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.7.2 at Annex IX includes similar information that is produced by the OECD TG 414 on one species. The following aspects are covered: 1) prenatal developmental toxicity, 2) maternal toxicity, and 3) maintenance of pregnancy.

All the sources of information you provided are described as investigating the key investigations. However, the study summaries provided by you on the sources of information are very limited and does not allow ECHA to assess the validity or relevance of the test any further.

In addition, the reliability of these sources of information is significantly affected by the deficiencies identified in section 1 of the Appendix on Reasons common to several requests.

Taken together, none of the sources of information provide information on the key investigations. In addition, 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 requirements are 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[3] administration of the Substance.

3. Long-term toxicity testing on fish

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 key studies (1995) on the Substance, 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 215;
iii. 1 QSAR predictions (EPA ECOSAR 1.1) for the Substance;
iv. 1 QSAR predictions (EPA ECOSAR 1.1) for an analogue substance (Sodium isobutyl xanthate, EC: 246-805-2, CAS: 25306-75-6).

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 Reasons common to several requests sections 1 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.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.2 at Annex VII includes similar information that is produced by the OECD TG 210. Therefore the following requirements must be met:

- parameters related to the survival and development of fish in early life stages from the stage of fertilized egg until the juvenile life-stage following exposure to the test substance are measured, including:
  1) the stage of embryonic development at the start of the test, and
  2) hatching of fertilized eggs and survival of embryos, larvae and juvenile fish, and
  3) the appearance and behaviour of larvae and juvenile fish, and
  4) the weight and length of fish at the end of the test.

The sources of information you provided do not investigate these key investigations. Therefore, they do not provide relevant information that would contribute to the conclusion on these key investigations.

In addition, the reliability of these sources of information is significantly affected by the deficiencies identified in section 1 of the Appendix on Reasons common to several requests.

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

Taken together, none of the sources of information provide information on the key investigations. In addition, 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 one source of information alone 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 requirements are not fulfilled.

Appendix D: Reasons to request information required under Annex X of REACH

1. Pre-natal developmental toxicity study 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 of REACH Regulation, providing the information mentioned in section 2 of Appendix C.

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

Based on the above, the information you provided do not fulfil the information requirement.

Information on study design
A PNDT study according to the OECD TG 414 study should be performed in the rabbit or rat as the preferred second species, depending on the species tested in the first PNDT study (request in section 2 of Appendix C).

The study shall be performed with oral[4] administration of the Substance.

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

Appendix E: 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[5].

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[6].

[5] https://echa.europa.eu/practical-guides
[6] https://echa.europa.eu/manuals

Appendix F: Procedure

The information requirement for an Extended one-generation reproductive toxicity study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the Sub-chronic toxicity study (90-day) requested in the present decision is provided; due to the fact that the results from the 90-day study is needed for the design of the EOGRTS. Similarly the information requirement for a Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) is not addressed in this decision; as the EOGRTS will cover the same parameters.

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 24 June 2020.

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

ECHA did not receive any comments within the commenting period.

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

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

Appendix G: List of references - ECHA Guidance[7] 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)[8]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[8]

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[9]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

[7] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[8] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[9] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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

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

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

Appendix H: Addressees of this decision and their corresponding information requirements

You must provide the information requested in this decision for all REACH Annexes applicable to you, except for REACH 2008 LTD. and SNF SA who must provide the information requested in this decision only for the information requirements for which they have not opted out.

These are:
(1) REACH 2008 LTD: (i) surface tension, (ii) justification for an adaptation of a Short-term repeated dose toxicity (28 days) via oral route based on the results of the Sub-chronic toxicity study (90 days), and (iii) sub-chronic toxicity study (90-day) via oral route;
(2) SNF SA: short-term toxicity testing on aquatic invertebrates.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[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.