~~Confidential~~

Helsinki, 10 November 2021

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

Date of submission of the dossier subject to this decision
12/04/2013

Registered substance subject to this decision ("the Substance")
Substance name: Potassium isopentyl dithiocarbonate
EC number: 213-180-2
CAS number: 928-70-1

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***15 February 2024***.

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

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

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

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

1. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats

2. 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. Transgenic rodent somatic and germ cell gene mutation assays (Annex IX, Section 8.4., column 2; test method: OECD TG 488 from 2020) in transgenic mice or rats, oral route on the following tissues: liver and glandular stomach; germ cells and duodenum must be harvested and stored for up to 5 years. Duodenum must be analysed if the results of the glandular stomach and of the liver are negative or inconclusive

   or

   In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 2; test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum

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

3. 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)

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

Reasons for the request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendices entitled "Reasons to request information required under Annexes VII to IX of REACH", respectively.

Information required depends on your tonnage band

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

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

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

How to comply with your information requirements

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

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

Appeal

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

Failure to comply

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

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

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

Appendix on Reasons common to several requests

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

You seek to adapt the following standard information requirements by applying (a) read-across approach(es) in accordance with Annex XI, Section 1.5:

- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

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

Grouping of substances and read-across approach

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

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[2] and related documents[3, 4].

A. Predictions for toxicological properties

You have provided a read-across justification document in CSR and in different sections of IUCLID.

You read-across between the analogue substances,

1) Carbon disulphide, EC 200-843-6, CAS 75-15-0;
2) 3-Methyl-butan-1-ol, EC 204-633-5, CAS 123-51-3;
3) Pentan-1-ol, EC 200-752-1, 71-41-0;
4) Potassium O-butyl dithiocarbonate (CAS 871-58-9; EC 212-808-2);

as source substances and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties: and "*This substance is hydrolytically unstable. As it is used in water solutions the systemic adverse effects are related to the main degradation products. It will decompose in water releasing mainly carbon disulphide and particular alcohols (3-methyl-butan-1-ol and pentan-1-ol). The decomposition rate is dependent on the pH, temperature and the concentration of the*

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

[3] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)

[4] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: https://doi.org/10.2823/794394

substance in water solutions. […] *Since CS2 is the most volatile and the most hazardous degradation product, it is the driving force for the hazard assessment of the target substance."* and *"xanthates can be considered as a group of substances which have structural similarity and similar behaviour in contact with water and in the physiological processes, their irritation as well as acute and systemic adverse effects to human health are similar. Therefore, […] the read-across data from the analogue xanthates is used to evaluate the irritation, and short term and/or long-term toxicological effects of the target substance"*

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

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

Based on the study/ies you provided with the source substance 4) ECHA understands that you predict the properties of the Substance for repeated dose toxicity also using a read-across hypothesis which

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

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

1. Supporting information

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

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

a. Missing information on the formation of common compound

As indicated above, one of your read-across hypothesis (1) is based on the (bio)transformation of the Substance and of the source substance(s) to a common compound(s). In this context, information characterising the rate and extent of the transformation of the Substance and of the source substance(s) is necessary to confirm the formation of the proposed common transformation product and to assess the impact of the exposure to the parent compounds.

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

In the absence of this information, you have not provided supporting evidence establishing

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

that the proposed common transformation product is formed as assumed in your read-across hypothesis. Therefore, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

b. Missing information to compare properties of the analogue substances

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

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

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

2. Adequacy and reliability of source study

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

i. be adequate for the purpose of classification and labelling and/or risk assessment;
ii. have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);
iii. cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

Specifically, this information must be available in the form of endpoint study records (robust study summaries) in the technical IUCLID dossier for all endpoints which are covered by the read-across adaptation, and for all source substances.

Your dossier does not contain any source studies for the source substances 1), 2) and 3) listed under **A.** above.

In the absence of robust study summaries for all relevant source substances under each endpoint for which a read-across adaptation is attempted, ECHA is unable to independently assess whether the criteria i), ii) and iii) above are met.

B. Predictions for ecotoxicological properties

1) Aquatic toxicity

You have provided a read-across justification document in CSR and in different sections of IUCLID.

You read-across between the analogue substances 1), 3),

5) Potassium *O*-pentyldithiocarbonate, EC 220-329-5, CAS 2720-73-2
6) Potassium *O*-isobutyldithiocarbonate, EC 235-837-2, CAS 13001-46-2

as source substances and the Substance as target substance.

You have provided the following reasonings for the prediction of aquatic toxicity: *"Target substance is hydrolytically unstable. It will decompose in the presence of water. In neutral to alkaline media, it will release carbon disulphide, particular alcohols (3-methylbutan-1-ol and pentan-1-ol) and carbonates and dithiocarbonates. Carbon disulphide is the major and the most critical decomposition product of the substance. As the target substance is an unstable compound, the apparent toxicity reflects to the toxicity of the degradation products. In the environment, the abiotic degradation by hydrolysis is also the driving force for the fate and pathways of the target substance. Therefore, the environmental properties of the degradation products are included in the chemical safety assessment to evaluate the fate and pathways of the target substance." and " As the xanthates can be considered as a group of substances which have structural similarity and similar behaviour in contact with water and in the physiological processes, their hydrolysis and biodegradation as well as ecotoxicological adverse effects to aquatic organisms are expected to be similar. Therefore, and in order to avoid the unnecessary animal testing, the read-across data from the analogue xanthates is used to evaluate the short-term and long-term toxicity to fish."*.

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

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

Based on the study/ies you provided with the source substances 5) and 6) ECHA understands that you predict the properties of the Substance for aquatic toxicity using a read-across hypothesis which

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

ECHA notes the following shortcoming(s) with regards to prediction(s) of aquatic toxicity.

Adequacy and reliability of source study

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

i. be adequate for the purpose of classification and labelling and/or risk assessment;
ii. have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);

You have used in your read-across approach different source studies for short-term and long-term toxicity testing on fish, listed in Appendixes B.2 and C.4.

All studies you have included do not provide an adequate coverage of validity criteria expected to be investigated. Therefore, all provided source studies do not include relevant, reliable and adequate information to support your read-across hypothesis.

Therefore, ECHA considers that the criteria i) and ii) above are not met.

C. Conclusions on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substance. Therefore, your adaptation does not

comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

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

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

EC 807-374-1 Isoamyl xanthate
EC 205-439-3 Potassium O-ethyl dithiocarbonate
EC 205-443-5 Proxan-sodium
EC 235-837-2 Potassium O-isobutyl dithiocarbonate
EC 220-977-9 S-allyl O-pentyl dithiocarbonate
EC 220-329-5 Potassium O-pentyl dithiocarbonate

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

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

2. Assessment of your substance-tailored exposure-driven testing adaptation under Annex XI, Section 3.2 (a)

You have sought to adapt the standard information requirements according to Annex XI, Section 3.2 (a) Substance-tailored exposure-driven testing for the following endpoints:

- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

As stated in Annex XI, Section 3, testing in accordance with Sections 8.6 and 8.7 of Annex VIII and in accordance with Annexes IX and X may be omitted based on the exposure scenario(s) developed in the CSR. For this purpose, the manufacturer or importer must provide an adequate and scientifically-supported justification based on a thorough and rigorous exposure assessment in accordance with Section 5 of Annex I and communicate the specific conditions of use through the supply chain.

In this context, one of the criteria that must be met is set out under Section 3.2(a) of Annex XI. According to that criterion, the manufacturer or importer shall demonstrate and document three cumulative conditions concerning i) the results of the exposure assessment; ii) the derivation of a suitable, relevant and appropriate DNEL or a PNEC and; iii) the comparison of the derived DNEL or PNEC with the results of the exposure assessment.

You have provided an adaptation in Section 7.8 of your technical dossier, and you conclude that "*according to the risk characterisation the amounts of CS2 released from the substance*

do not trigger the target substance to be classified as reproduction toxic, and the CSA does not indicate to further investigate the developmental toxicity of the target substance."

You provided the following justification for the adaptation:
"*This substance is hydrolytically unstable. As it is used in water solutions the systemic adverse effects are related to the main degradation products. It will decompose in water releasing mainly carbon disulphide and particular alcohols (3-methyl-butan-1-ol and pentan-1-ol). The decomposition rate is dependent on the pH, temperature and the concentration of the substance in water solutions. The loss of xanthates for 10 %, 25 % and 40 % water solutions to volatile degradation products at 20 °C is measured to be 1.1 to 0.5 %, and at 30 °C 2.7 to 2.0 %, respectively. The release of CS2 during the storage from the 25 % water solution is estimated to be below 0.2 % per day at 20 °C and 30 °C (Aeroxanthate handbook 1972). Carbon disulphide as the major degradation product has the harmonized classification for Repro 2 with SCL of 1 % and for STOT-RE (SCL for STOT-RE 2 is 0.2% and SCL for STOT-RE 1 is 1%). Since CS2 is the most volatile and the most hazardous degradation product, it is the driving force for the hazard assessment of the target substance. Therefore, the exposure to CS2 via inhalation has been taken into account in the quantitative exposure assessment (sections 9&10 of CSR). The exposure assessment was done based on the monitoring data from end user sites as well as based on the modelled exposure estimates. According to the results of the assessment, the risks were considered controlled when appropriate OCs and RMMs with PPEs and safety practices are applied*."

In section 10 of your CSR you conclude "The combined risk characterization ratio via inhalation to CS2 vapours formed during preparation and use of xanthate waters solutions from charging and mixing (PROC 8b and PROC 3) is RCR = [redacted] indicating the safe use of the substance (estimation based on ECETOC TRA model calculations)."

ECHA notes the following shortcomings with regards to your adaptation according to Annex XI, Section 3.2 (a) Substance-tailored exposure-driven testing:

i. Inappropriate DNEL derivation

The second cumulative condition under Annex XI, Section 3.2(a) requires that a suitable DNEL or a PNEC can be derived from results of available test data for the Substance taking full account of the increased uncertainty resulting from the omission of the information requirement, and that DNEL or PNEC is relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes.

ECHA notes that you refer to the national OEL of the degradation product (carbon disulphide) of the the Substance. Workers will be exposed to the the Substance, as there is slow degradation on the the Substance according to the data provided in section 7.8 of your technical dossier. Exposure may also take place via the dermal route or via ingestion. In the context of omitting Annex IX data requirements, this is not a suitable way to demonstrate that exposure and risk of toxic effects from the the Substance are absent or negligible.

Additionally ECHA notes that you refer to national OELs of carbon disulphide from Finland, Germany, Sweden and the United Kingdom rather than a DNEL in your dossier. The use of these OELs has not been scientifically motivated in your dossier (Guidance R8-13); "*A registrant cannot use a national OEL in place of a DNEL without an evaluation of the scientific background for setting the OEL. However, in cases where toxicological information and evaluations of health effects used for setting the OEL are documented and available, this may, as for IOELs, be used and taken into account in deriving the DNEL. In this evaluation, the approach used for setting the OEL should be compared to the approach for deriving DNELs as described in the main body of this chapter, and any differences in approach should be taken*

into account." In particular, the OEL you refer to (15mg/m^3 set by Finland) is not based on reproductive or developmental toxicity, nor is it based on testing of the the Substance but rather neurotoxicity of carbon disulphide.

Therefore, the second cumulative condition under Annex XI, Section 3.2(a) cannot be fulfilled.

ii. Comparison of DNEL with the results of the exposure assessment

The third cumulative condition under Annex XI, Section 3.2(a) requires that the comparison of the derived DNEL or PNEC with the results of the exposure assessment shows that exposures are always well below the derived DNEL or PNEC.

As described in 'Inappropriate DNEL derivation" you do not have a suitable DNEL to compare with the exposure estimates or the exposure measurements included in your dossier.

Therefore, the third cumulative condition under Annex XI, Section 3.2(a) cannot be fulfilled.

Based on the above, the information you provided in the dossier does not meet the general rules for adaptation of Annex XI, Section 3.2(a), as two of the cumulative conditions of that adaptation are not currently fulfilled.

Therefore your adaptation is rejected.

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

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

- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

Your weight of evidence adaptation raises the same decifiencies irrespective of the information requirement for which it is invoked. Accordingly, ECHA addressed these deficiencies in the present Appendix, before assessing the specific standard information requirements in the following appendices.

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

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

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

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

Regarding the sub-chronic toxicity study, while you state that "*the weight of evidence approach is used to determine the hazard caused by repeated oral administration of potassium isoamyl xanthate*", you have not included a justification with an assessment, integration and weighing of the individual sources of information for relevance, reliability, consistency and results, and subsequently decided whether they together provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

1. Reliability of the read across approach

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

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

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

1. Surface tension

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

You have provided the following information for this endpoint:

i. An adaptation: "The substance [redacted]. When [redacted], surface activity is not a desired property of the substane."

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

> According to Column 2 of Annex VII, Section 7.6, Surface tension study only need to be conducted if i) based on structure, surface activity is expected or can be predicted, or ii) surface activity is a desired property of the material. If the water solubility is below 1 mg/l at 20°C the test does not need to be conducted.
>
> ECHA cannot relate your adaptation statement to any Column 2 adaptation for this endpoint. In addition, based on the structure of the Substance, surface activity can be expected, because the Substance has hydrophilic and lipophilic moieties.

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

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

1. Screening for reproductive/developmental toxicity

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

While you have not specifically claimed the adaptation, ECHA understands you have adapted this information requirement using substance-tailored exposure-driven testing adaptation under Annex XI, Section 3.2 (a). You have not provided any studies for the information requirement.

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

As explained in Section 2 of the Appendix common to several requests, your substance-tailored exposure-driven testing adaptation is rejected and the information requirement is not fulfilled.

A study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed in rats with oral[6] administration of the Substance.

Comments to the draft decision

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

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

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

ECHA acknowledges the possibilities to waive the information requirement if the criteria of Annex VIII, Section 8.7.1, Column 2 fourth indent is met. However, the information provided in your dossier does not comply with REACH Regulation. Therefore, ECHA is requesting information. Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "*How to act in Dossier Evaluation)*."

In any case, it is in your discretion to generate and provide the necessary supporting information in order to justify any adaptation. If you do so, you are responsible for demonstrating the fulfilment of the specific requirements of Annexes VII-IX and/or the

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

general requirements of Annex XI to REACH. ECHA will evaluate the latest submission provided after the deadline of this decision.

2. Short-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

You have provided the following information:

i. OECD TG 203, key study on source substance potassium O-isobutyl dithiocarbonate (EC 235-837-2) ([redacted] 1987)
ii. Experimental supporting study on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) with no guideline information provided ([redacted] 1986)
iii. Experimental supporting study on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) with no guideline information provided ([redacted] 1974)
iv. Experimental supporting study on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) with no guideline information provided ([redacted] 1976)
v. Experimental supporting study on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) on *Notropis atherinoide* with no guideline information provided ([redacted] 1977)
vi. Experimental supporting study on source substance potassium O-pentyl dithiocarbonate (EC 220-329-5) on *Pimephales promelas* with no guideline information provided ([redacted] 1977)
vii. EPA test methodology, supporting study on source substance pentan-1-ol (EC 200-752-1) ([redacted] 1986)
viii. Experimental supporting study on source substance carbon disulphide (EC 200-843-6) with no guideline information provided (IUCLID Dataset, 2000)

We have assessed this information and identified the following issues:

To fulfil the information requirement, a study must comply with OECD TG 203 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following requirements must be met:

- mortality in the control(s) is ≤ 10% (or one fish, if fewer than 10 control fish are tested) at the end of the test;
- the analytical measurement of test concentrations is conducted;
- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;
- in static tests, if the concentrations of the test material:
  1) are expected to remain within ± 20 % of the nominal, then the test substance concentration is determined (in one replicate) in the highest and lowest test concentrations, and a concentration around the expected LC50 at the beginning and end of the test,
  2) are not expected to remain within ± 20 % of the nominal, then the test substance concentration is determined (in one replicate) in all concentrations at the beginning, at 48 hours and at the end of the test;
- in semi-static tests, test concentrations are measured at least twice over one exposure period (before and after renewal of test solutions). If the concentrations of the test material:

1) are expected to remain within ± 20 % of the nominal, then the test substance concentration is determined) in the highest and lowest test concentrations, and a concentration around the expected LC50.
2) are expected to decline by more than 20%, analytical monitoring is conducted on all test concentrations with an additional determinations on the other exposure period(s);

- in flow-through tests, test concentrations are measured before initiation of the exposure and with sufficient frequency of sampling during exposure to document the stability of the exposure to the test material;

Your registration dossier provides several studies (i.e. i-iv and viii) showing the following:

- mortality in the control(s) at the end of the test was not reported;
- no analytical measurement of test concentrations was conducted;

Besides, the study vii does not provide information on the mortality of the controls.

You have assigned the endpoint study records v. and vi. ([redacted] 1977) with a reliability 3, and further explained it to be due to these "*not ontaining the details of the test materials, methods and study results, including statistics and controls. Detailed references to the xanthate studies conducted by the* [redacted] *are not cited nor available*." ECHA agrees with your assessment. Therefore, this study record is not reliable.

Based on the above, the validity criteria of OECD TG 203 are not met in any of the studies.

On this basis, the information requirement is not fulfilled.

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

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

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

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

Study design

The Substance is difficult to test due to the reported technical function of being a flotation agent in the CSR, indicating surface active properties. OECD TG 203 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve

and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 203. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solutions.

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

1. **In vivo mammalian alkaline comet assay; or Transgenic rodent somatic and germ cell gene mutation assays**

Under Annex IX, Section 8.4, column 2 of REACH, the information requirement for an appropriate *in vivo* somatic cell genotoxicity study is triggered if 1) there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and 2) there are no appropriate results already available from an *in vivo* somatic cell genotoxicity study.

The ECHA guidance R.7a states that following a positive result in an *in vitro* test, "*adequately conducted somatic cell in vivo testing is required to ascertain if this potential can be expressed in vivo. In cases where it can be sufficiently deduced that a positive in vitro finding is not relevant for in vivo situations (e.g. due to the effect of the test substances on pH or cell viability, in vitro-specific metabolism: see also Section R.7.7.4.1), or where a clear threshold mechanism coming into play only at high concentrations that will not be reached in vivo has been identified (e.g. damage to non-DNA targets at high concentrations), in vivo testing will not be necessary.*"

In relation to the first condition, your dossier contains positive results for the *in vitro* gene mutation study in mammalian cells which raise the concern for gene mutation. You also provided the following considerations explaining that the genotoxic potential of the substance cannot be expressed *in vivo*:

"*This study shows evidence on the mutagenicity potential for the potassium isoamyl xanthate. However, in vitro tests generally present crucial limitations which affect the usefulness of the assays to predict mutagenicity/genotoxicity potential of a substance in vivo in mammals and especially in humans.*

These limitations are:
- lack of a "human like" metabolic capacity of the cell lines used
- absence of toxicokinetics
- oversensitivity compared to in vivo situations – low specificity
- sometimes the use of cell lines that are not relevant to predict genotoxic endpoints at target organs

Due to these limitations, no single in vitro test can be used for the evaluation of the mutagenicity/genotoxicity potential of a substance.

Furthemore, potassium isoamyl xanthate hydrolyses when in contact with water or moisture releasing alcohol, carbon disulphide, potassium carbonate and potassium trithiocarbonate. These decomposition products are not classified for mutagenicity. Neither of other xanthates have classification for mutagenicity.

Based on the above facts, potassium isoamyl xanthate is not considered to be mutagenic in humans."

ECHA acknowledges that no single *in vitro* test can be used for the evaluation of the mutagenicity/genotoxicity potential because of the limitations indicated by you. Adequately conducted somatic cell *in vivo* testing is therefore required to ascertain if the genotoxic potential can be expressed *in vivo*, because no data from an appropriate *in vivo* somatic cell genotoxicity study is available in the dossier.

ECHA considers that an appropriate *in vivo* follow up mutagenicity study is necessary to address the concern identified *in vitro*.

In relation to the second condition, your dossier contains no data from an *in vivo* somatic cell genotoxicity study.

Therefore, the conditions set out in Annex IX, Section 8.4, column 2 are met and the information requirement for an appropriate *in vivo* somatic cell genotoxicity study is triggered.

i. Test selection

According to the ECHA Guidance Chapter R.7a[7], the transgenic rodent somatic and germ cell gene mutation assay ("TGR assay", OECD TG 488) and the *in vivo* mammalian alkaline comet assay ("comet assay", OECD TG 489) are suitable to follow up a positive *in vitro* result on gene mutation.

ii. Test design

In case you decide to perform the comet assay according to the test method OECD TG 489, the test must be performed in rats. Having considered the anticipated routes of human exposure and the need for adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

In line with the test method OECD TG 489, the test must be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

In case you decide to perform the TGR assay, according to the test method OECD TG 488, the test must be performed in transgenic mice or rats and the test substance is usually administered orally.

Based on the recent update of OECD TG 488 (2020), you are requested to follow the new 28+28d regimen, as it permits the testing of mutations in somatic tissues and as well as in tubule germ cells from the same animals. This updated version provides for a transitional period for the new version. However, ECHA is aware that testing according to the updated OECD TG is already available from CROs and the new study design would provide meaningful germ cell data, so this decision requires the application of the new version.

According to the test method OECD TG 488, the test must be performed by analysing tissues from liver as slowly proliferating tissue and primary site of xenobiotic metabolism, glandular stomach and duodenum as rapidly proliferating tissue and site of direct contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for mutagenicity at the site of contact in the gastro-intestinal tract. However,

[7] ECHA Guidance Chapter R.7a, Section R.7.7.6.3

duodenum must be stored (at or below −70 ºC) until the analysis of liver and glandular stomach is completed; the duodenum must then be analysed only if the results obtained for the glandular stomach and for the liver are negative or inconclusive.

iii. Germ cells

A subsequent germ cell genotoxicity study (TGR/OECD TG 488, or CA on spermatogonia/OECD TG 483) may still be required under Annex IX of REACH, in case 1) an *in vivo* genotoxicity test on somatic cell is positive, and 2) no clear conclusion can be made on germ cell mutagenicity.

Therefore, in case you decide to perform the comet assay, you may consider to collect the male gonadal cells collected from the seminiferous tubules (as described by e.g. O'Brien *et al*.[8]) in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, in accordance to Annex IX, Section 8.4., column 2, you should consider analysing the slides prepared with gonadal cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

Therefore, in case you decide to perform the TGR, you must collect the male germ cells (from the seminiferous tubules) at the same time as the other tissues, in order to limit additional animal testing. According to the OECD 488 the tissues (or tissue homogenates) can be stored under specific conditions and used for DNA isolation for up to 5 years (at or below −70 ºC). This duration is sufficient to allow you or ECHA, in accordance to Annex IX, Section 8.4., column 2, to decide on the need for assessment of mutation frequency in the collected germ cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

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

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

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

You have provided the following source of information:

i) Subchronic toxicity study (1966) in rat on source substance potassium O-butyl dithiocarbonate (EC 212-808-2);

ECHA has assessed this information and identified the following issue(s):
Annex XI, Section 1.2 states that there may be sufficient weight of evidence "*from several independent sources of information*".

You have only provided one source of information.

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

[8] O'Brien, J.M., Beal, M.A., Gingerich, J.D., Soper, L., Douglas, G.R., Yauk, C.L., Marchetti, F. (2014) Transgenic Rodent Assay for Quantifying Male Germ Cell Mutant Frequency. J. Vis. Exp. (90), e51576, doi:10.3791/51576

The reliability of the source of information is significantly affected by the deficiencies identified in Section 3 of the Appendix on General considerations.

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

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017) Chapter R.7a, Section R.7.5.4.3 - is the most appropriate route of administration. No oral repeated dose toxicity study is available to evaluate systemic toxicity following oral administration. Hence, the test shall be performed by the oral route using the test method OECD TG 408.

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

Comments to the draft decision

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

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

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

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

3. Pre-natal developmental toxicity study in one species

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

You have adapted this information requirement by referring to Annex XI, without specifying the type of adaptation. Furthermore, you have not provided studies under the IUCLID section 7.8.2.

While you have not specifically claimed the adaptation, ECHA understands you have adapted this information requirement using substance-tailored exposure-driven testing adaptation under Annex XI, Section 3.2 (a).

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

As explained in Section 2 of the Appendix common to several requests, your substance-tailored exposure-driven testing adaptation is rejected and the information requirement is not fulfilled.

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[9] administration of the Substance.

In your comments on the draft decision you provide the same information for this endpoint as for request C.2. ECHA has replied to your comment under request C.2.

4. Long-term toxicity testing on fish

Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

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

i. Experimental study on source substance potassium O-pentyl dithiocarbonate (CAS 2720-73-2 / EC 220-329-5), guideline: Sprague, 1973 ([redacted] 1976), weight of evidence approach
ii. Experimental study on source substance potassium O-pentyl dithiocarbonate (CAS 2720-73-2 / EC 220-329-5), no standard guideline followed ([redacted] 1975), weight of evidence approach

As explained in Section 3 of the Appendix on Reasons common to several requests, the weight of evidence must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

We have assessed this information and identified the following issues:

To fulfil the information requirement, normally a study according to OECD TG 210 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test, must be provided. The key parameter investigated by this test is fish reproduction.

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

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

In addition, the reliability of the source of information is also affected by the following issue. In order to assess the validity of a test, at least information on the controls (e.g. overall survival of fertilised eggs in the controls) must be provided and analytical measurements of the test concentrations must be conducted.

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

Therefore validity criteria is not fulfilled.

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

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

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

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

We have assessed this information and identified the following issue:

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

Therefore, your adaptation is rejected.

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

OECD TG 210 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Section B.2.

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

A. Test methods, GLP requirements and reporting

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

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

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

B. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

1. Selection of the Test material(s)

   The Test Material used to generate the new data must be selected taking into account the following:
   - the variation in compositions reported by all members of the joint submission,
   - the boundary composition(s) of the Substance,
   - the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

2. Information on the Test Material needed in the updated dossier
   - You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   - The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[11].

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

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

A. Testing strategy for aquatic toxicity testing

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

Appendix F: Procedure

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

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

The compliance check was initiated on 17 January 2020.

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

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

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

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments and referred the modified draft decision to the Member State Committee.

You did not provide any comments on the proposed amendment(s).

The Member State Committee unanimously agreed on the draft decision in its MSC-75 written procedure. ECHA adopted the decision under Article 51(6) of REACH.

Appendix G: List of references - ECHA Guidance[12] and other supporting documents

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

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

Read-across assessment framework (RAAF, March 2017)[13]

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

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

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

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

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

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

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

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

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

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

OECD Guidance documents[14]

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

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

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

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

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

Appendix H: Addressees of this decision and the corresponding information requirements applicable to them

You must provide the information requested in this decision for all REACH Annexes applicable to you.

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