Helsinki, 10 March 2020

Addressees
Registrants of [redacted] listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
02/02/2019

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: 2'-acetonaphthone
EC number: 202-216-2
CAS number: 93-08-3

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

DECISION ON A COMPLIANCE CHECK

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

A. Requirements applicable to all the Registrants subject to Annex VII of REACH

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

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

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

B. Requirements applicable to all the Registrants subject to Annex VIII of REACH

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

2. Only if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained, In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method OECD TG 476 or TG 490) with the Substance

3. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method OECD 421) in rats, oral route with the Substance

4. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method OECD TG 203) with the Substance

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

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

- you have to comply with the requirements of Annex VII of REACH, if you have registered a substance at 1-10 tonnes per annum (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- you have to comply with the requirements of Annexes VII and VIII of REACH, if you have registered a substance at 10-100 tpa;

The Appendix on general considerations addresses common arguments that are applicable throughout the present decision while the other Appendices state the further reasons for the requests for information to fulfil the requirements set out in the respective Annexes of REACH.

The testing material used to perform the required studies shall be selected and reported in accordance with the specifications prescribed in Appendix Observations and technical guidance.

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

Appeal

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

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

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

Appendix on general considerations

Adaptations according to Annex XI

Your registration dossier contains adaptation arguments for the information requirements addressed in this decision (requests A.1 – B.4) either in the form of a weight-of-evidence approach according to Annex XI, Section 1.2., or predictions generated with QSAR models under Annex XI, Section 1.3. of the REACH Regulation. A list of references to ECHA Guidance documents containing further information on these adaptations are listed in Appendix E of this decision.

For each relevant endpoint, ECHA has assessed your adaptation arguments in line with the conditions specified in Annex XI of the REACH Regulation:

(i) For the use of adaptations using Weight of Evidence (WoE) according to Annex XI, Section 1.2., it should be demonstrated that there is sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while the information from each single source alone is regarded insufficient to support this notion.

A weight of evidence adaptation shall include an assessment of the relative values/weights of different pieces of the available information which is defined by e.g. the reliability of the data, consistency of results/data, nature and severity of effects, and relevance of the information for the given regulatory endpoint. Subsequently, the lines of evidence should be integrated considering their relative values or weights in order to draw a conclusion (ECHA Guidance R.4.4).

Adequate and reliable documentation shall be provided to describe your WoE approach, the assessment of relative weights of individual piece of information and the subsequent conclusions drawn.

Whenever sources of information derived from analogue substances are used as part of a WoE, the characterisation of the analogue substance(s) identified needs to be as detailed as possible and a reasoning needs to be provided to establish why information from analogue substance(s) can reliably be read-across.

(ii) 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.

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

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

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

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

You have adapted the standard information requirement under Annex XI, Section 1.2., Weight of evidence, by providing the following two endpoint study records and indicated the adequacy of studies as "weight of evidence":

i. Wild *et al,* 1983*: In vitro* gene mutation study in bacteria with the Substance. GLP status not specified. Negative in *S. typhimurium* strains: TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation. You assigned a reliability score of 2 to this study.

ii. Fujita *et al,* 1986*: In vitro* gene mutation study in bacteria with the Substance. GLP status not specified. Negative in *S. typhimurium* strains: TA97 and TA102 with and without metabolic activation. You assigned a reliability score of 4 to this study.

Furthermore, in your comments to the draft decision you have referred to:

iii. a study on the similar substance methyl-2-naphthyl ether. Negative in *S. typhimurium* strains: TA98, TA100, TA 102 TA1535, TA1537, with and without metabolic activation, and

iv. a study on the similar substance ethyl-2-naphthyl ether. Negative in *S. typhimurium* strains: TA98, TA100, TA 102 TA1535, TA1537, with and without metabolic activation.

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

Reliability of study (i)

Regarding the information under point (i), the provided study does not fulfil the requirements of an OECD TG 471 study (updated 1997) on its own, because the study does not include tests with strains *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101). One of these strains is a key parameter required in the current OECD TG 471 (1997). Therefore, the study does not provide all the data required in an OECD TG 471 study. Furthermore, the documentation of this study does not allow to assess its reliability as no information on the test concentrations and on the composition of the test material used in this study is provided.

In your comments to the draft decision you consider that paragraph 13 of the OECD TG 471 establishes a recommended combination of strains and that *"in order to detect cross-linking mutagens it may be preferable to include TA 102 or add a DNA repair-proficient strain of E.coli"*. You conclude that the use of these strains is not mandatory.

Our understanding of paragraph 13 of OECD TG 471, as adopted in 1997, differs from yours. This paragraph starts with 4 clear statements:

"At least five strains of bacteria should be used";
"These should include four strains of *S. typhimurium* (TA1535; TA1537 or TA97a or TA97; TA98; and TA100)";
"These four *S. typhimurium* strains have GC base pairs at the primary reversion site and it is known that they may not detect certain oxidising mutagens, cross-linking agents and hydrazines";
"Such substances may be detected by *E.coli* WP2 strains or *S. typhimurium* TA102 (19) which have an AT base pair at the primary reversion site".

Paragraph 13 then makes a clear conclusion: "Therefore the recommended combination of strains is:

1. *S. typhimurium* TA1535, and
2. *S. typhimurium* TA1537 or TA97 or TA97a, and
3. *S. typhimurium* TA98, and
4. *S. typhimurium* TA100, and
5. *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102".

In 1997, the wording of the OECD TG 471 was updated from "*At least four strains, TA 1535, TA 1537, TA 98 and TA 100 should be used [version 1983]*" to "*At least five strains of bacteria should be used [version 1997]*". The revised version of the guideline from 1997 clearly described the nature of the 5th strain. This 5th strain is now a key feature of the current OECD TG 471.

We consider that this paragraph should be read in relation to the fact that for the 5th strain there is a choice between *S. typhimurium* TA102 and *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101). So the meaning of this last sentence of paragraph 13 is that in case the aim of the Ames test is also to detect cross-linking mutagens, then the operator should include TA102 (as the 5th strain) or add DNA repair-proficient strain of *E. coli*, e.g. *E. coli* WP2 or *E. coli* WP2 (pKM101) (if *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101) has been chosen as the 5th strain). The information submitted to fulfil the information requirement of Annex VII, 8.4.1 of the REACH Regulation is expected to investigate the potential of the Substance to act as cross-linking mutagen and therefore information obtained from testing *on S. typhimurium* TA 102 or a DNA repair-proficient strain of *E.coli* is required.

Our understanding of paragraph 13 of the OECD TG 471 (1997) is in agreement with the way all experienced and accredited CROs have been performing the Ames test since the OECD TG 471 was updated in 1997

Reliability of study (ii)

Regarding the information under point (ii), you have disregarded the study by assigning a reliability score of 4 to the reported study. ECHA agrees that the documentation provided for this study does not allow to assess its reliability. In particular, no information on the presence or absence of positive and negative controls and on the outcome of the tests using these controls is provided. No information on the composition of the test material used in this study is provided. Therefore, ECHA cannot consider the report a reliable source of information contributing to weight of evidence for the presence or absence of the particular dangerous property.

Use of information from similar substances in WoE adaptations

In your comments to the draft decision you identified information on the similar substances methyl-2-naphthyl ether (CAS 93-04-9) and ethyl-2-naphthyl ether (CAS 93-18-5) and considered this information in your adaptation.

Justification for the relevance of information

As indicated in the Appendix on General considerations, and in accordance with the ECHA Guidance[2], a scientific justification needs to establish why the toxicological or ecotoxicological properties of the Substance can be determined from information on the 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 attached a document to your comments to the draft decision intended to justify the use of information obtained on the similar substance CAS 93-04-9 in your WoE adaptation for this endpoint. This document presents a set of physico-chemical properties and alerts obtained from the QSAR Toolbox v3.4 for the Substance and for each of these similar substances. On the basis of this information you derive conclusions on the structural similarities, similarities in physico-chemical properties and similarities in the alert profiles between the Substance and each of the above similar substance. You conclude that "*Based on structural similarity, reactivity, physical–chemical properties, and general mechanistic approach, the above were identified as read-across materials with sufficient data for toxicological evaluation*".

Provided that the applicability domain is appropriate, the results from using QSAR models may be used in a weight of evidence analysis where such data are considered alongside other relevant data. Considering the complexity and amount of information needed from various function and parameters to evaluate endpoint such as genotoxicity, QSAR predictions alone do not establish that structurally similar substances have similar properties for this endpoint. Therefore the reliability of these predictions cannot be assessed. Moreover, you have not provided robust relevant scientific information other than these alerts to establish that the genotoxicity of the Substance can be determined from information on the similar substance methyl-2-naphthyl ether (CAS 93-04-9). Therefore the information from study iii. is considered as not relevant for this WoE adaptation.

In your comments you also refer to available information on the similar substance 2-ethoxynaphtalene (CAS 93-18-5). You have not provided any justification in your dossier or in your comments establishing the relevance of the information on 2-ethoxynaphtalene (CAS 93-18-5) for the Substance. Therefore the information from study iv. is considered as not relevant for this WoE adaptation.

Reliability of information on similar substances

Under Article 10(a)(vii) of the REACH Regulation, a technical dossier must include "*robust study summaries of the information derived from the application of Annexes VII to XI, if required under Annex I*". Annex I, Section 1.1.4/3.1.5 of REACH states that robust study summaries are "*required of all key data used in the hazard assessment*".

In the document attached to your comments to the draft decision you have identified studies conducted with the similar substances methyl-2-naphthyl ether (CAS 93-04-9) and ethyl-2-

[2] ECHA Guidance R.4, Section R.4.3.2.2.

naphthyl ether (CAS 93-18-5) that you intend to use as sources of information in your weight of evidence approach and provided high-level narratives presenting these studies.

You have not provided robust study summaries for any for these source studies. In particular you have not provided detailed information on the methods, results and conclusions of these studies allowing for an independent assessment of the studies. In the absence of such information, we cannot assess the reliability of the information from these studies.

Requirement for documentation of the WoE adaptation

With reference to the conditions for adaptations under Annex XI, Section 1.2, which ECHA further explained in the Appendix on general considerations above, it is not apparent how the relative value and weight of the above pieces of the available information alone or considered together would be sufficient to allow conclusions that the Substance has or has not the dangerous property investigated in a *In vitro* gene mutation study in bacteria.

You have in particular not provided documentation to your WoE approach which would include an assessment of the relative weights of the individual pieces of information and the subsequent conclusions drawn.

In each of the endpoint-specific sections of your comments to the draft decision you described the sources of information that you considered in your WoE adaptation and concluded that with this information you consider that you have been able to fulfil the different information requirements.

Whilst these summaries can be regarded as integrated summaries of the data sets, you have not communicated and documented in a robust and transparent manner your considerations on the relevance, reliability of the individual sources of information. No critical assessment of their relative weight and of the overall adequacy of the data set in the context of these WoE is included in the documentation of your adaptations.

Conclusion

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

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

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

You have provided a key study "Short term toxicity of test chemical to daphnia" (2017) conducted according to OECD TG 202.

According to Article 13(4) of REACH, ecotoxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP). According to Article 141(2), Article 13 applies from entry into application of the REACH Regulation on 1 June 2008.

The study you provided is not performed in compliance with GLP.

In your comments to the draft decision, you confirmed that the key study was not performed

according to GLP.

i. In addition, in your comments to the draft decision you have referred to: A study on the similar substance 2-methoxynaphthalene (CAS 93-04-9 / EC No. 202-213-6) according to OECD TG 202. No test material characterization, no GLP, no robust study summary (RSS) and no bibliographical reference were provided, and
ii. A study on the similar substance 1-Hydroxynaphthalene (CAS 90-15-3 / EC No. 201-969-4. However, no results were reported of the study on this substance.

Finally, in your comments to the draft decision you claim that the data from all studies reported in your comments confirms the classification of the Substance as Aquatic Chronic 3 according to the CLP regulation and on that basis you ask ECHA to remove the request of the study from the draft decision.

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

a) Use of information from similar substances in WoE adaptations

Justification for the relevance of information

As indicated in the Appendix on General considerations, and in accordance with the ECHA Guidance R.4, Section R.4.3.2.2., a scientific justification needs to establish why the toxicological or ecotoxicological properties of the Substance can be determined from information on the 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 attached a document to your comments to the draft decision intended to justify the use of information obtained on the similar substance 2-methoxynaphthalene (CAS 93-04-9) in your WoE adaptation for this endpoint. This document presents a set of physico-chemical properties and alerts obtained from the QSAR Toolbox v3.4 for the Substance and for each of these similar substances. On the basis of this information you derive conclusions on the structural similarities, similarities in physico-chemical properties and similarities in the alert profiles between the Substance and the above similar substance. You conclude that "*Based on structural similarity, reactivity, physical-chemical properties, and general mechanistic approach, the above were identified as read-across materials with sufficient data for toxicological evaluation*".

Provided that the applicability domain is appropriate, the results from using QSAR models may be used in a weight of evidence analysis where such data are considered alongside other relevant data. Considering the complexity and amount of information needed from various function and parameters to evaluate endpoints such as short-term toxicity to aquatic invertebrates QSAR predictions alone do not establish that structurally similar substances have similar properties for these endpoints. You have not provided robust scientific information on why the differences between these substances should not influence the toxicological/ ecotoxicological properties of the Substance, and including relevant and reliable studies of comparable design and duration establishing why the ecotoxicological properties of the Substance can be determined from information on the similar substance 2-methoxynaphthalene (CAS 93-04-9). Therefore the information from study i. is considered as not relevant for this WoE adaptation.

You have not provided any data from the indicated study on the similar substance 1-

Hydroxynaphthalene (CAS 90-15-3). Therefore the information from study ii. is considered as not relevant for this WoE adaptation.

Reliability of information on similar substances

Under Article 10(a)(vii) of the REACH Regulation, a technical dossier must include "*robust study summaries of the information derived from the application of Annexes VII to XI, if required under Annex I*". Annex I, Section 1.1.4/3.1.5 of REACH states that robust study summaries are "*required of all key data used in the hazard assessment*".

In the document attached to your comments to the draft decision you have identified studies conducted with the similar substances 2-methoxynaphthalene (CAS 93-04-9) and 1-Hydroxynaphthalene (CAS 90-15-3) that you intend to use as sources of information in your weight of evidence approach and provided high-level narrative presenting the study 2-methoxynaphthalene (CAS 93-04-9).

You have not provided robust study summaries for any for these source studies. In particular you have not provided detailed information on the methods, results and conclusions of these studies allowing for an independent assessment of the studies. In the absence of such information, we cannot assess the reliability of the information from these studies.

Requirement for documentation of the WoE adaptation

With reference to the conditions for adaptations under Annex XI, Section 1.2, which ECHA further explained in the Appendix on general considerations above, it is not apparent how the relative value and weight of the above pieces of the available information alone or considered together would be sufficient to allow conclusions that the Substance has or has not the dangerous property investigated in a short-term toxicity study on aquatic invertebrates.

You have in particular not provided documentation to your WoE approach which would include an assessment of the relative weights of the individual pieces of information and the subsequent conclusions drawn. In each of the endpoint-specific sections of your comments to the draft decision you described the sources of information that you considered in your WoE adaptation and concluded that with this information you consider that you have been able to fulfil the different information requirements.

Whilst these summaries can be regarded as integrated summaries of the data sets, you have not communicated and documented in a robust and transparent manner your considerations on the relevance, reliability of the individual sources of information. No critical assessment of their relative weight and of the overall adequacy of the data set in the context of these WoE is included in the documentation of your adaptations.

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

b) Use of classification as an adaptation

Classification as Aquatic Chronic 3 under the CLP regulation is not a valid waiver in Annex VII, Section 9.1, column 2 or under the General rules for adaptation under Annex XI.

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

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

You have provided a key study "Effect of test chemical on fresh water algae" (2017) conducted according to OECD TG 201.

According to Article 13(4) of REACH, ecotoxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP). According to Article 141(2), Article 13 applies from entry into application of the REACH Regulation on 1 June 2008.

The study you provided is not performed in compliance with GLP.

In your comments to the draft decision, you confirmed that the key study was not performed according to GLP.

In addition, in your comments to the draft decision you have referred to:

i. A study on the similar substance 2-methoxynaphthalene (CAS 93-04-9 / EC No. 202-213-6) according to OECD TG 201. No test material characterization, no GLP, no robust study summary (RSS) and no bibliographical reference were provided.

Finally, in your comments to the draft decision you claim that the data from all studies reported in your comments confirms the classification of the Substance as Aquatic Chronic 2 according to the CLP regulation and on that basis you ask ECHA to remove the request of the study from the draft decision.

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

a) Use of information from similar substances in WoE adaptations

Justification for the relevance of information

As indicated in the Appendix on General considerations, and in accordance with the ECHA Guidance R.4, Section R.4.3.2.2., a scientific justification needs to establish why the toxicological or ecotoxicological properties of the Substance can be determined from information on the 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 attached a document to your comments to the draft decision intended to justify the use of information obtained on the similar substance CAS 93-04-9 in your WoE adaptation for this endpoint. This document presents a set of physico-chemical properties and alerts obtained from the QSAR Toolbox v3.4 for the Substance and for each of these similar substances. On the basis of this information you derive conclusions on the structural similarities, similarities in physico-chemical properties and similarities in the alert profiles between the Substance and the above similar substance. You conclude that "*Based on structural similarity, reactivity, physical-chemical properties, and general mechanistic approach, the above were identified as read-across materials with sufficient data for toxicological evaluation*".

Provided that the applicability domain is appropriate, the results from using QSAR models may be used in a weight of evidence analysis where such data are considered alongside other relevant data. Considering the complexity and amount of information needed from various function and parameters to evaluate endpoints such as growth inhibition on aquatic plants QSAR predictions alone do not establish that structurally similar substances have similar properties for these endpoints. You have not provided robust scientific information on why the differences between these substances should not influence the toxicological/ ecotoxicological properties of the Substance, and including relevant and reliable studies of comparable design and duration establishing why the ecotoxicological properties of the Substance can be determined from information on the similar substance 2-methoxynaphthalene (CAS 93-04-9). Therefore the information from study i. is considered as not relevant for this WoE adaptation.

Reliability of information on similar substances

Under Article 10(a)(vii) of the REACH Regulation, a technical dossier must include "*robust study summaries of the information derived from the application of Annexes VII to XI, if required under Annex I*". Annex I, Section 1.1.4/3.1.5 of REACH states that robust study summaries are "*required of all key data used in the hazard assessment*".

In the document attached to your comments to the draft decision you have identified study conducted with the similar substances 2-methoxynaphthalene (CAS 93-04-9) that you intend to use as sources of information in your weight of evidence approach and provided high-level narrative presenting the study 2-methoxynaphthalene (CAS 93-04-9).

You have not provided robust study summary for this source study. In particular you have not provided detailed information on the methods, results and conclusions of this study allowing for an independent assessment of the study. In the absence of such information, we cannot assess the reliability of the information from this study.

Requirement for documentation of the WoE adaptation

With reference to the conditions for adaptations under Annex XI, Section 1.2, which ECHA further explained in the Appendix on general considerations above, it is not apparent how the relative value and weight of the above pieces of the available information alone or considered together would be sufficient to allow conclusions that the Substance has or has not the dangerous property investigated in a growth inhibition study on aquatic plants.

You have in particular not provided documentation to your WoE approach which would include an assessment of the relative weights of the individual pieces of information and the subsequent conclusions drawn. In each of the endpoint-specific sections of your comments to the draft decision you described the sources of information that you considered in your WoE adaptation and concluded that with this information you consider that you have been able to fulfil the different information requirements.

Whilst these summaries can be regarded as integrated summaries of the data sets, you have not communicated and documented in a robust and transparent manner your considerations on the relevance, reliability of the individual sources of information. No critical assessment of their relative weight and of the overall adequacy of the data set in the context of these WoE is included in the documentation of your adaptations.

Conclusion

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

b) Use of classification as an adaptation

Classification as Aquatic Chronic 2 under the CLP regulation is not a valid waiver in Annex VII, Section 9.1, column 2 or under the General rules for adaptation under Annex XI.

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

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

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

An *In vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is a standard information requirement in Annex VIII to the REACH Regulation.

You have adapted the standard information requirement under Annex XI, Section 1.2., Weight of evidence, by providing the following endpoint study records and indicated the adequacy of studies as "weight of evidence":

i. [redacted] 2018; in vitro mammalian chromosome aberration test according to the OECD TG 473 using the similar substance 2-methoxynaphtalene (CAS 93-04-9; EC 202-213-6). GLP status not specified. Negative results were obtained in the presence and in the absence of metabolic activation. You have assigned a reliability score of 1 to this study.
ii. National Institute of Technology and Evaluation, 2017; in vitro mammalian chromosome aberration test according to the OECD TG 473 using the similar substance 2-(2-methylpropoxy)naphtalene (CAS 2173-57-1; EC 218-529-2). GLP status not specified. Negative results were obtained in the presence and in the absence of metabolic activation. You have assigned a reliability score of 2 to this study.

Furthermore, in your comments to the draft decision you have referred to the following studies included in your dossier:

iii. Wild et al, 1983; *in vivo* micronucleus study in mice using the Substance. Negative results. Guideline not specified. GLP status not specified;
iv. Wild et al, 1983; Drosophila sex-linked recessive lethal test using the Substance. Negative results. Guideline not specified. GLP status not specified.

We have assessed this information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation and identified the following general issues.

Use of information from similar substances in WoE adaptations

Justification for the relevance of information

As explained above in the Appendix on general considerations, characterisation of the analogue substance(s) and a reasoning needs to be provided to establish why information from analogue substance(s) can reliably contribute to the WoE. You have not provided:

- detailed information on the identity of the source substance(s), in particular the composition of the test material(s);
- any reasoning establishing why information from analogue substance(s) can reliably contribute to the WoE.

You have attached a document to your comments to the draft decision intended to justify the use of information obtained on the similar substances 2-methoxynaphtalene (CAS 93-04-9) and 2-(2-methylpropoxy)naphtalene (CAS 2173-57-1) in your WoE adaptation for this endpoint. This document presents a set of physico-chemical properties and alerts obtained from the QSAR Toolbox v3.4 for the Substance and for each of these similar substances. On the basis of this information you derive conclusions on the structural similarities, similarities in physico-chemical properties and similarities in the alert profiles between the Substance and each of the above similar substance. You conclude that "*Based on structural similarity, reactivity, physical-chemical properties, and general mechanistic approach, the above were identified as read-across materials with sufficient data for toxicological evaluation*".

Provided that the applicability domain is appropriate, the results from using QSAR models may be used in a weight of evidence analysis where such data are considered alongside other relevant data. Considering the complexity and amount of information needed from various function and parameters to evaluate endpoint such as genotoxicity, QSAR predictions alone do not establish that structurally similar substances have similar properties for this endpoint. Therefore the reliability of these predictions cannot be assessed. Moreover, you have not provided robust relevant scientific information other than these alerts to establish that the genotoxicity of the Substance can be determined from information on the similar substances 2-methoxynaphtalene (CAS 93-04-9) and 2-(2-methylpropoxy)naphtalene (CAS 2173-57-1).

Therefore the information from study i. and ii. is considered as not relevant for this WoE adaptation.

- any information explaining why certain information may contribute to inform on the potential of the test substance to cause structural and numerical chromosome aberrations

In your comments to the draft decision you further referred to the results obtained in a drosophila sex-linked recessive lethal test conducted with the Substance (study iv. above). You considered that these results contibute to the WoE adaptation for this information requirement and that they support your conclusion of "non mutagenic effects of the test chemical suggesting no safety concern for mutations in humans".

Study iv. is a drosophila sex-linked recessive lethal test. The information requirement of Annex VIII, 8.4.2 requires information from an in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study. These studies inform on the potential of the test substance to cause structural and numerical chromosome aberrations. The study you have provided detects mutations in germ cells of drosophilia. It does not inform on the potential of the test substance to cause structural and numerical chromosome aberrations. Therefore, the information from the study iv. is not considered as relevant for this WoE adaptation.

Reliability of information on similar substances

In addition, the GLP status of the studies is identified as "not specified". The uncertainty of the conditions under which the studies have been conducted affects the assessment of the reliability of this information. Reliability is an important parameter of the WoE, as explained in point i. of the Appendix on general considerations above. You have not explained how this limitation affects the use of this information as part of the WoE approach.

In your comments to the draft decision you additionaly referred to the "*predominently negative*" results obtained in an *in vivo* micronucleus study conducted with the Substance (study iii above). You considered that these results contibute to the WoE adaptation for this information requirement and that they support your conclusion of "*non mutagenic effects of the test chemical suggesting no safety concern for mutations in humans*".

ECHA has assessed this information and has observed the following issues:

The ECHA Guidance R.4, Section R.4.2 sets out the criteria for assessing the reliability of information provided as part of WoE adaptations. Deviations from the recognised test method are identified as an element potentially impacting the reliability of the information.

- Study iii. is an *in vivo* mammalian erythoricyte micronucleus test. The corresponding recognised test method is the OECD TG 474. The OECD TG 474 requires that a group of animal be treated with a positive control substance in each test. This positive control should reliably produce a detectable increase in micronucleus frequency over the spontaneous level. Based on the information provided in the technical dossier, no positive control was included in the design of the study iii. In the absence of such control, it is not possible to confirm that the test system used to conduct this test could reliably detect increases in micronucleus frequency. Therefore, the information from the study iii. is considered unreliable.

Requirement for documentation of the WoE adaptation

With reference to the conditions for adaptations under Annex XI, Section 1.2, which ECHA further explained in the Appendix on general considerations above, it is not apparent how the relative value and weight of the above pieces of the available information alone or considered together would be sufficient to allow conclusions that the Substance has or has not the dangerous property investigated in an *In vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study.

You have in particular not provided documentation to your WoE approach which would include an assessment of relative weights of the individual pieces of information and the subsequent conclusions drawn.

Also the additional information provided in your comments on the draft decision do not meet the requirement for the documentation of such an assessment. In each of the endpoint-specific sections of your comments to the draft decision you described the sources of information that you considered in your WoE adaptation and concluded that with this information you consider that you have been able to fulfil the different information requirements. However, whilst these summaries can be regarded as integrated summaries of the data sets, you have not communicated and documented in a robust and transparent manner your considerations on the relevance, reliability of the individual sources of information. No critical assessment of their relative weight and of the overall adequacy of the data set in the context of these WoE is included in the documentation of your adaptations.

Conclusion

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

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

An *In vitro* gene mutation study in mammalian cells is an information requirement in Annex VIII to the REACH Regulation, if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained.

The registration dossier does not contain any appropriate study record in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2., as explained above under A.1 and B.1. Provided that the studies requested under A.1 and B.1 have negative results, information on In vitro gene mutation in mammalian cells will need to be provided in the dossier.

You have adapted the standard information requirement under Annex XI, Section 1.2., Weight of evidence, by providing the following two endpoint study records and indicating the adequacy of the studies as "weight of evidence":

i. [redacted] 2015; in vitro mammalian cell gene mutation test according to the OECD TG 476 using the similar substance 2-methoxynaphtalene (CAS 93-04-9; EC 202-213-6). GLP status not specified. Negative results were obtained in the presence and in the absence of metabolic activation. You have assigned a reliability score of 1 to this study.

ii. US National Library of Medicine, 2018; in vitro mammalian cell gene mutation test according to the OECD TG 476 using the similar substance 1-phenylethan-1-one (CAS 98-86-2; EC 202-708-7). GLP status not specified. Negative results were obtained in the presence and in the absence of metabolic activation. You have assigned a reliability score of 2 to this study.

Furthermore, in your comments to the draft decision you have referred to the following studies included in your dossier:

iii. Wild et al, 1983; *in vivo* micronucleus study in mice using the Substance. Negative results. Guideline not specified. GLP status not specified;

iv. Wild et al, 1983; Drosophila sex-linked recessive lethal test using the Substance. Negative results. Guideline not specified. GLP status not specified.

We have assessed this information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation and identified the following general issues.

Use of information from similar substances in WoE adaptations

Justification for the relevance of information

Regarding both studies mentioned in your registration dossier, i. and ii., and as explained in above Appendix on general considerations, characterisation of the analogue substance(s) and a reasoning needs to be provided to establish why information from analogue substance(s) can reliably contribute to the WoE. You have not provided:

- detailed information on the identity of the source substance(s) in particular the composition of the test material(s);
- any reasoning establishing why information from analogue substance(s) can reliably contribute to the WoE.

You have attached a document to your comments to the draft decision intended to justify the use of information obtained on the similar substances 2-methoxynaphtalene (CAS 93-04-9) and 1-phenylethan-1-one (CAS 98-86-2) in your WoE adaptation for this endpoint. This document presents a set of physico-chemical properties and alerts obtained from the QSAR Toolbox v3.4 for the Substance and for each of these similar substances. On the basis of this information you derive conclusions on the structural similarities, similarities in physico-chemical properties and similarities in the alert profiles between the Substance and each of the above similar substance. You conclude that "*Based on structural similarity, reactivity, physical–chemical properties, and general mechanistic approach, the above were identified as read-across materials with sufficient data for toxicological evaluation*".

Provided that the applicability domain is appropriate, the results from using QSAR models may be used in a weight of evidence analysis where such data are considered alongside other relevant data. Considering the complexity and amount of information needed from various function and parameters to evaluate endpoint such as genotoxicity, QSAR predictions alone do not establish that structurally similar substances have similar properties for this endpoint. Therefore the reliability of these predictions cannot be assessed. Moreover, you have not provided robust relevant scientific information other than these alerts to establish that the genotoxicity of the Substance can be determined from information on the similar substances 2-methoxynaphtalene (CAS 93-04-9) and 1-phenylethan-1-one (CAS 98-86-2). Therefore the information from studies i. and ii. is considered as not relevant for this WoE adaptation.

In your comments to the draft decision you further referred to the "*predominently negative*" results obtained in a drosophila sex-linked recessive lethal test conducted with the Substance (study iv. above). You considered that these results contribute to the WoE adaptation for this information requirement and that they support your conclusion of "*non mutagenic effects of the test chemical suggesting no safety concern for mutations in humans*".

The information requirement of Annex VIII, 8.4.3 requires information from an *in vitro* gene mutation study in mammalian cells. The study iv. is a drosophila sex-linked recessive lethal test. This test was conducted in insects, i.e. a non-mammalian test system, and therefore does not inform on the potential of the test material to cause gene mutation in mammalian cells. Therefore, the information from the study iv. is not considered as relevant for this WoE adaptation.

Reliability of information on similar substances

The GLP status of the studies is further identified as "not specified". The uncertainty of the conditions under which the studies have been conducted affects the assessment of the reliability of this information. Reliability is an important parameter of the WoE, as explained in the Appendix on general considerations. You have not explained how this limitation affects the use of this information as part of the WoE approach. In your comments to the draft decision you further referred to the "*predominently negative*" results obtained in an *in vivo* micronucleus study conducted with the Substance (study iii and iv) You considered that these results contibute to the WoE adaptation for this information requirement and that they support your conclusion of "*non mutagenic effects of the test chemical suggesting no safety concern for mutations in humans*".

ECHA has assessed this information and has identified the following issues:

The ECHA Guidance R.4, Section R.4.2 sets out the criteria for assessing the reliability of information provided as part of WoE adaptations. Deviations from the recognised test method are identified as an element potentially impacting the reliability of the information.

- Study iii. is an *in vivo* mammalian erythrocyte micronucleus test. This test detects stuctural and numerical chromosome aberrations. It does not inform on the potential of the test substance to cause gene mutations. Therefore, the information from the study iii. is not considered as relevant for your adaptation of this information requirement.

In addition, under Article 10(a)(vii) of the REACH Regulation, a technical dossier must include "*robust study summaries of the information derived from the application of Annexes VII to XI, if required under Annex I*". Annex I, Section 1.1.4/3.1.5 of REACH states that robust study summaries are "*required of all key data used in the hazard assessment*".

- For study iv. you have not provided a robust study summary for this study. The level of information provided to describe the test conditions and to present the test results of study iv. in your dossier is very limited. In particular you have not provided detailed information on the methods, results and conclusions of these studies allowing for an independent assessment of the studies. In the absence of such information, we cannot assess the reliability of the information from the study iv.

Requirement for documentation of the WoE adaptation

With reference to the conditions for adaptations under Annex XI, Section 1.2, which ECHA explained in the Appendix on general considerations above, it is not apparent how the relative value and weight of the above pieces of the available information alone or considered together would be sufficient to allow conclusions that the Substance has or has not the dangerous property investigated in an *In vitro* gene mutation study in mammalian cells.

You have in particular not provided documentation to your WoE approach which would include an assessment of relative weights of the individual pieces of information and the subsequent conclusions drawn.

Also the additional information provided in your comments on the draft decision do not meet the requirement for the documentation of such an assessment. In each of the endpoint-specific sections of your comments to the draft decision you described the sources of information that you considered in your WoE adaptation and concluded that with this information you consider that you have been able to fulfil the different information requirements. However,whilst these summaries can be regarded as integrated summaries of the data sets, you have not communicated and documented in a robust and transparent manner your considerations on the relevance, reliability of the individual sources of information. No critical assessment of their relative weight and of the overall adequacy of the data set in the context of these WoE is included in the documentation of your adaptations.

Conclusion

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

3. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.);

Screening for reproductive/developmental toxicity (test method OECD TG 421 or 422) is a standard information requirement in Annex VIII to the REACH Regulation if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from *in vitro* methods that the substance may be a developmental toxicant. No such evidence is presented in the dossier.

You have adapted the standard information under Annex XI, Section 1.2., Weight of evidence, by providing the following information on analogue substances and indicated the adequacy of the studies as "weight-of-evidence":

i. MHW Report, 2001; one-generation reproductive toxicity in rats according to the OECD TG 415 using the similar substance 2-naphtol (CAS 135-19-3; EC 205-182-7). GLP compliant. NOAEL parental: 160 mg/kg/d; NOAEL F1: 40 mg/kg/d; You have assigned a reliability score of 2 to this study;
ii. MHW Report, 2012; one-generation reproductive toxicity in rats according to the OECD TG 415 using the similar substance 3-Hydroxy-2-naphthoic acid (CAS 92-70-6; EC 202-180-8). GLP compliant. NOAEL parental: 200 mg/kg/d; NOAEL F1: 50 mg/kg/d; You have assigned a reliability score of 2 to this study;
iii. EFSA, 2010; one-generation reproductive toxicity in rats according to the OECD TG 415 using the similar substance 2-naphtyloxyacetic acid (CAS 120-23-0; EC 204-380-0). GLP status not specified. NOAEL parental: 153.8 mg/kg/d; NOAEL F1: 153.8 mg/kg/d; You have assigned a reliability score of 4 to this study;

Furthermore, in your comments to the draft decision you have referred to the following study:

iv. Combined repeated dose toxicity and reproduction/developmental screening study (OECD TG 422) conducted with the similar substance acetophenone (CAS 98-86-2; EC 202-708-7) in rats via the oral route (gavage).

We have assessed this information according to the requirements of Annex XI, Section 1.2 of the REACH Regulation and identified the following general issues.

Use of information from similar substances in WoE adaptations: Justification for the relevance of information

Regarding the information i.-iii., and as explained in above Appendix on general considerations, characterisation of the analogue substance(s) and a reasoning needs to be provided to establish why information from analogue substance(s) can reliably contribute to the WoE. You have not provided:

- detailed information on the identity of the source substance(s) in particular the composition of the test material(s);
- any reasoning establishing why information from analogue substance(s) can reliably contribute to the WoE.

Furthermore, the following observations are noted for the different studies:

- MHW Report, 2001: evidence of reproductive toxicity has been obtained in this study. 2-naphtol has been identified as impairing spermatogenesis in the parent animals in

the mid and high doses. Reduced litter size, reduced fetal weight, reduced number of live pups and reduced offspring survival have been observed in the high dose group. You have not documented in your dossier your assessment of these findings and their contribution to your WoE approach.

- MHW Report, 2012: increased incidence of abnormalities in testis have been reported in the high dose group animals in this study. You have not documented in your dossier your assessment of these findings and their contribution to your WoE approach.

You have attached a document to your comments to the draft decision intended to justify the use of information obtained on the similar substances 2-naphtol (CAS 135-19-3), 3-Hydroxy-2-naphthoic acid (CAS 92-70-6), 2-naphtyloxyacetic acid (CAS 120-23-0) and acetophenone (CAS 98-86-2) in your WoE adaptation for this endpoint. This document presents a set of physico-chemical properties and alerts obtained from the QSAR Toolbox v3.4 for the Substance and for each of these similar substances. On the basis of this information you derive conclusions on the structural similarities, similarities in physico-chemical properties and similarities in the alert profiles between the Substance and each of the above similar substance. You conclude that "*Based on structural similarity, reactivity, physical–chemical properties, and general mechanistic approach, the above were identified as read-across materials with sufficient data for toxicological evaluation*".

Provided that the applicability domain is appropriate, the results from using QSAR models may be used in a weight of evidence analysis where such data are considered alongside other relevant data[3]. Considering the complexity and amount of information needed from various function and parameters to evaluate endpoints such as reproductive and developmental toxicity QSAR predictions alone do not establish that structurally similar substances have similar properties for these endpoints. You have not provided robust scientific information, including relevant and reliable studies of comparable design and duration, establishing why the toxicological properties of the Substance can be determined from information on the similar substances 2-naphtol (CAS 135-19-3), 3-Hydroxy-2-naphthoic acid (CAS 92-70-6), 2-naphtyloxyacetic acid (CAS 120-23-0) and acetophenone (CAS 98-86-2). Therefore the information from studies i.-iv. is considered as not relevant for this WoE adaptation.

Reliability of study iv.

Under Article 10(a)(vii) of the REACH Regulation, a technical dossier must include "*robust study summaries of the information derived from the application of Annexes VII to XI, if required under Annex I*". Annex I, Section 1.1.4/3.1.5 of REACH states that robust study summaries (RSS) are "*required of all key data used in the hazard assessment*".

In the document attached to your comments to the draft decision you have referred to a combined repeated dose toxicity and reproduction/developmental screening study (OECD TG 422) conducted with the similar substance acetophenone (CAS 98-86-2) in rats via the oral route (gavage) (study iv.). You intend to use this study as a source of information in your weight of evidence approach. In your comments to the draft decision you have provided a high-level narrative presenting the design of this study and the reproductive/developmental toxicity findings detected. An RSS for this study is included in the section on repeated-dose toxicity of your technical dossier.

[3] ECHA Guidance R.7a, Section R.7.6.4.1.2

The RSS included in your dossier reports on the repeated-dose toxicity aspects of this study only. You have not provided an RSS presenting the reproductive and developmental toxicity investigations conducted as part of this study and the related findings in your technical dossier. In particular you have not provided detailed information on the method, results and conclusions of this study allowing for an independent assessment of the study. In the absence of such information, we cannot assess the reliability of the information from this study. Therefore, this information is considered as unreliable in the context of this weight of evidence adaptation.

Requirement for documentation of the WoE adaptation

With reference to the conditions for adaptations under Annex XI, Section 1.2, which ECHA explained in the Appendix on general considerations above, it is not apparent how the relative value and weight of the above pieces of the available information alone or considered together would be sufficient to allow conclusions that the Substance has or has not the dangerous property investigated in a screening for reproductive/developmental toxicity test.

You have not provided in your dossier a documentation of your WoE approach in your dossier which would include an assessment of relative weights of the individual pieces of information and the subsequent conclusions drawn.

In the endpoint-specific section of your comments to the draft decision you have provided your assessment of the information from studies i.-iv. You concluded that "*Conclusive data from several in vivo experimental studies indicate that the prenatal exposure to 2-acetonaphthone interferes with the normal development of the offspring, reduce offspring viability and produce birth defects in the absence of obvious maternal toxicity. Hence, 2-acetonaphthone is likely to be reprotoxicant and consequently classified as Category 2 for reproductive and developmental toxicity according to CLP criteria*". You consider that the information requirement of Annex VIII, 8.7.1 for a screening for reproductive/developmental toxicity test can be waived as a consequence of the self-classification of the Substance as Repr. 2.

As indicated above, you have not established why the information on the similar substances 2-naphtol (CAS 135-19-3), 3-Hydroxy-2-naphthoic acid (CAS 92-70-6), 2-naphtyloxyacetic acid (CAS 120-23-0) and acetophenone (CAS 98-86-2) is relevant to conclude on the hazardous properties of the Substance.
According to the information provided in your dossier and in your comments, under the conditions of study i. 2-naphtol (CAS 135-19-3) impaired spermatogenesis in the parent animals in the mid and high doses, caused reduced litter size, reduced fetal weight, reduced number of live pups and reduced offspring survival. Based on the information included in your comments, acetophenone (CAS 98-86-2) caused a significant decrease in the total number of live born pups and a reduced viability index in the high dose group of study iv. As indicated above, in the absence of a robust study summary for study iv., the information obtained from this study is considered unreliable in the context of this weight of evidence adaptation.

You consider that in the conditions of the studies ii. and iii. on the similar substances 3-Hydroxy-2-naphthoic acid (CAS 92-70-6) and 2-naphtyloxyacetic acid (CAS 120-23-0), respectively, provided in your dossier, these substances did not cause reproductive toxicity.
Based on this information, we understand that the individual pieces of information on similar substances that you have compiled in the context of this WoE adaptation do not provide consistent results. However in your comments you have concluded from this data set that the

Substance is likely to be reprotoxicant. You have not elaborated on the relative value and weight of the different pieces of information in deriving this conclusion. Furthermore, whilst you consider that the Substance merits classification as Repr. 2, you have not provided a justification establishing that the Substance may not cause more severe reproductive toxicity than that observed with the similar substances.

Furthermore, ECHA notes that according to the provisions of Annex VIII, Section 8.7, column 2, the information requirement for a screening for reproductive/developmental toxicity test may be waived if the substance is classified as toxic for reproduction category 1A or 1B: may damage fertility/the unborn child. Classification as toxic to reproduction category 2 is not a specific adaptation possibility for this information requirement.

Conclusion

There is not sufficient evidence, based on any source of information alone or considered together that the Substance is or is not toxic to reproduction or a developmental toxicant. Therefore, your adaptation according to Annex XI, Section 1.2. is rejected and the information requirement is not fulfilled.

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

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

You have provided a key study "Acute toxicity study of the test chemical to fish" (2017) conducted according to OECD TG 203.

According to Article 13(4) of REACH, ecotoxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP). According to Article 141(2), Article 13 applies from entry into application of the REACH Regulation on 1 June 2008.

The study you provided is not performed in compliance with GLP.

In your comments to the draft decision, you confirmed that the above key study was not performed according to GLP.

In addition, in your comments to the draft decision you have referred to:

i. A study on the similar substance 1-Nitronaphthalene (CAS 86-57-7 / EC No. 201-684-5). No test material characterization, no guideline, no GLP, no robust study summary (RSS) and no bibliographical reference were provided.
ii. A study on the similar substance (2-naphthyloxy)acetic acid (CAS 120-23-0 / EC No. 204-380-0). No test material characterization, no guideline, no GLP, no robust study summary (RSS) and no bibliographical reference were provided.

Finally, in your comments to the draft decision you claim that the data from all studies reported in your comments confirms the classification of the Substance as Aquatic Chronic 2 according to the CLP regulation and on that basis you ask ECHA to remove the request of the study from the draft decision.

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

a) Use of information from similar substances in WoE adaptations

Justification for the relevance of information

As indicated in the Appendix on General considerations, and in accordance with the ECHA Guidance R.4, Section R.4.3.2.2., a scientific justification needs to establish why the toxicological or ecotoxicological properties of the Substance can be determined from information on the 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 attached a document to your comments to the draft decision intended to justify the use of information obtained on the similar substances CAS 86-57-7 and CAS 120-23-0 in your WoE adaptation for this endpoint. This document presents a set of physico-chemical properties and alerts obtained from the QSAR Toolbox v3.4 for the Substance and for each of these similar substances. On the basis of this information you derive conclusions on the structural similarities, similarities in physico-chemical properties and similarities in the alert profiles between the Substance and the above similar substance. You conclude that "*Based on structural similarity, reactivity, physical–chemical properties, and general mechanistic approach, the above were identified as read-across materials with sufficient data for toxicological evaluation*".

Provided that the applicability domain is appropriate, the results from using QSAR models may be used in a weight of evidence analysis where such data are considered alongside other relevant data. Considering the complexity and amount of information needed from various function and parameters to evaluate endpoints such as short-term toxicity to fish QSAR predictions alone do not establish that structurally similar substances have similar properties for these endpoints. You have not provided robust scientific information on why the differences between these substances should not influence the toxicological/ ecotoxicological properties of the Substance, and including relevant and reliable studies of comparable design and duration establishing why the ecotoxicological properties of the Substance can be determined from information on the similar substances 1-Nitronaphthalene (CAS 86-57-7) and (2-naphthyloxy)acetic acid (CAS 120-23-0). Therefore the information from studies i. and ii. is considered as not relevant for this WoE adaptation.

Reliability of information on similar substances

Under Article 10(a)(vii) of the REACH Regulation, a technical dossier must include "*robust study summaries of the information derived from the application of Annexes VII to XI, if required under Annex I*". Annex I, Section 1.1.4/3.1.5 of REACH states that robust study summaries are "*required of all key data used in the hazard assessment*".

In the document attached to your comments to the draft decision you have identified studies conducted with the similar substances 1-Nitronaphthalene (CAS 86-57-7) and (2-naphthyloxy)acetic acid (CAS 120-23-0) that you intend to use as sources of information in your weight of evidence approach and provided high-level narratives presenting the above studies.

You have however not provided robust study summaries for any for these source studies. In particular you have not provided detailed information on the methods, results and conclusions

of these studies allowing for an independent assessment of the studies. In the absence of such information, we cannot assess the reliability of the information from these studies.

Requirement for documentation of the WoE adaptation

With reference to the conditions for adaptations under Annex XI, Section 1.2, which ECHA further explained in the Appendix on general considerations above, it is not apparent how the relative value and weight of the above pieces of the available information alone or considered together would be sufficient to allow conclusions that the Substance has or has not the dangerous property investigated in a short-term toxicity study on aquatic invertebrates.

You have in particular not provided documentation to your WoE approach which would include an assessment of the relative weights of the individual pieces of information and the subsequent conclusions drawn. In each of the endpoint-specific sections of your comments to the draft decision you described the sources of information that you considered in your WoE adaptation and concluded that with this information you consider that you have been able to fulfil the different information requirements.

Whilst these summaries can be regarded as integrated summaries of the data sets, you have not communicated and documented in a robust and transparent manner your considerations on the relevance, reliability of the individual sources of information. No critical assessment of their relative weight and of the overall adequacy of the data set in the context of these WoE is included in the documentation of your adaptations.

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

b) Use of classification as an adaptation

Classification as Aquatic Chronic 2 under the CLP regulation is not a valid waiver in Annex VIII, Section 9.1.3, column 2 or under the General rules for adaptation under Annex XI.

Appendix C: Procedural history

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

The compliance check was initiated on 16/01/2019.

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

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

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

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

Appendix D: Observations and technical guidance

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

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

3. Test guidelines, GLP requirements and reporting

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

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

   According to Article 10 (a) (vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide: 'How to report robust study summaries[4]'.

4. Test material

   Selection of the test material(s)

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

   While selecting the test material you must take into account the impact of each constituent/impurity is known to have or could have on the test results for the endpoint to be assessed. For example, if a constituent/impurity of the Substance is known to have an impact on (eco)toxicity, the selected test material must contain that constituent/ impurity.

   Technical reporting of the test material

   The composition of the selected test material must be reported in the respective endpoint study record, under the Test material section. The composition must include all constituents of the test material and their concentration values. Without such detailed reporting, ECHA may not be able to confirm that the test material is relevant for the Substance and to all the registrants of the Substance.

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

Technical instructions are available in the manual "How to prepare registration and PPORD dossiers" on the ECHA website (https://echa.europa.eu/manuals).

5. List of references of the ECHA Guidance documents[5]

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

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

ECHA Read-across assessment framework (RAAF, March 2017)[6]

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.

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.

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

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

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