EUROPEAN CHEMICALS AGENCY

~~Confidential~~

Helsinki, 18 January 2021

Addressees
Registrants of JS_Benzalacetone as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
26 March 2020

Registered substance subject to this decision ("the Substance")
Substance name: 4-phenylbutenone
EC number: 204-555-1
CAS number: 122-57-6

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 ***24 October 2022***.

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

A. 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 (gavage), in rats

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

1. 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)

2. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)

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

Reasons for the requests are explained in the following appendices:

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

Information required depends on your tonnage band

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

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

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

How to comply with your information requirements

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

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

Appeal

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

Failure to comply

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

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

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

Appendix on Reasons common to several requests

1. Assessment of your QSAR adaptation under Annex XI, Section 1.3

You seek to adapt the following standard information requirements by applying (Q)SAR approaches in accordance with Annex XI, Section 1.3:

- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

You have provided QSAR predictions for these endpoints according to ECOSAR v1.11 (a) based on the models for '*neutral organics*' and (b) for '*Vinyl/Allyl Ketones*'.

Under Annex XI to REACH, Section 1.3., the study may be omitted using (Q)SAR results if the following cumulative conditions are met:

1. the prediction needs to be derived from a scientifically valid model, and
2. the substance must fall within the applicability domain of the model, and
3. results need to be adequate for the purpose of risk assessment or classification and labelling, and
4. adequate and reliable documentation of the method must be provided.

With regard to these conditions, we have identified the following issues:

A. The predictions are not reliable

ECHA Guidance R.6.1.5.3. specifies that a prediction must be reliable and thus the following conditions must be met:

- the substance falls within descriptor, structural, mechanistic and metabolic domain of the model;
- the reliability of the prediction is demonstrated, taking into account, for example, the consistency of calculated and the measured values for related endpoints.

You report the following predictions from the '*neutral organics*' model:

- Prediction of short-term toxicity on aquatic organisms:
  - Fish: 96h-LC50 of 111.1 mg/l
  - Daphnia: 48h-EC50 of 63.3 mg/l
  - Algae: 96h-ErC50 of 47.8mg/l
- Prediction of long-term toxicity on aquatic organisms:
  - Fish: 30d-ChV of 10.9 mg/l (as the geometric mean of the LOEC and NOEC)
  - Daphnia: 21d-ChV of 6.2 mg/l

You report the following predictions from the '*Vinyl/Allyl Ketones*' model:

- Prediction of short-term toxicity on aquatic organisms:
  - Fish: 96h-LC50 of 139.2 mg/l
  - Daphnia: 48h-EC50 of 91.5 mg/l
  - Algae: 96h-ErC50 of 54.4 mg/l
- Prediction of long-term toxicity on aquatic organisms:
  - Fish: 30d-ChV of 41.0 mg/l
  - Daphnia: 21d-ChV of 14.1 mg/l

On the predictions for long-term to aquatic invertebrates, you state the following: "*The toxicity value was estimated through application of acute-to-chronic ratios. Since the SAR to derive the acute value is not considered reliable, the chronic result bears also high uncertainty*".

Your registration dossier also provides reliable studies on acute toxicity to aquatic organisms showing the following:

- Fish: 96h-LC50 of 5.7 mg/l ([redacted], 2006) and of 6.5mg/l ([redacted], 1993)
- Daphnia: 48h-EC50 of 15 mg/l ([redacted], 2006)
- Algae: 72h-ErC50 of 0.55 mg/l ([redacted], 2010)

Based on the above, you have not demonstrated the reliability of the predictions of the '*neutral organics*' model for the following reasons:

- the software predicts that the Substance belongs to the Vinyl/Allyl Ketones class, not the neutral organics class. Hence the Substance does not fall within the mechanistic domain of the model;
- the predictions for short-term aquatic toxicity are not consistent with available reliable experimental data as measured effect values are well below predicted values. You have provided no justification for that difference in an endpoint closely related to long-term aquatic toxicity.

In addition, you have not demonstrated the reliability of the predictions of the '*Vinyl/Allyl Ketones*' for the substance for the following reason:

- the prediction for short-term aquatic toxicity are not consistent with available reliable experimental data as measured effect values are well below predicted values. You have provided no justification for that difference in an endpoint closely related to long-term aquatic toxicity.

B. *The scientific validity of the 'Vinyl/Allyl Ketones' model is not established*

ECHA Guidance R.6.1.3. specifies that, to be considered scientifically valid, a (Q)SAR model must fulfil the principles described in the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2). The fourth OECD principle requires that appropriate measures of the internal performance (*i.e.* goodness-of-fit and robustness using the learning data set) and predictivity (using a test data set) of the model are available. To estimate the robustness of a model, the ratio of the number of objects (*i.e.* chemicals) in the training set over the number of selected variables or descriptors included in the model must be at least five.

On the predictions for long-term to fish, you state the following: "[the predictions do] *not appear reliable since the training set of the SAR for Vinyl/Allyl Ketones only consists of data on 1 compound".*

As the '*Vinyl/Allyl Ketones*' model for long-term toxicity to fish relies on a training set including a single chemical and a single variable (logKow), the ratio of the number of objects (i.e. chemicals) over the number of selected variables is below five. Therefore, the robustness of the model cannot be determined and the fourth OECD principle is not met.

Therefore, your adaptations for the two standard information requirements above are rejected.

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

1. Screening study for reproductive/developmental toxicity

A Screening for reproductive/developmental toxicity study is an information requirement under Annex VIII to REACH (Section 8.7.3.), if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have adapted this information requirement under Annex XI, Section 1.2 of REACH ('Weight of evidence'). In support of your adaptation, you have provided four sub-chronic (90 days) repeated dose toxicity studies in rats and mice, both via the oral (feeding) and dermal routes with the Substance ([redacted], 2012).

In your comments to the draft decision you also submitted a adaptation for this information requirement under Annex VIII, Section 8.7.1., column 2, first paragraph, fourth indent.

We have assessed the information and identified the following issues:

A. Weight of evidence adaptation

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 (not) a particular (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 whether the Substance has the (hazardous) 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 adaptation. However, 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 (not) a particular hazardous property investigated by the required study.

Irrespective of the above mentioned deficiencies on the documentation, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided sources of information.

To fulfil this information requirement, normally a study performed according to EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be provided. OECD TGs 421/422 require to investigate the following key elements: 1) sexual function and fertility, 2) toxicity to offspring, and 3) systemic toxicity.

Key elements/key investigations: *sexual function and fertility, toxicity to offspring, and systemic toxicity*

1) Sexual function and fertility

Sexual function and fertility on both sexes must include information on mating, fertility, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, organ weights and histopathology of reproductive organs and tissues, litter sizes, nursing performance and other potential aspects of sexual function and fertility.

The four studies you submitted provide limited information on sexual function and fertility. More specifically, they provide information only on oestrous cyclicity and sperm parameters and they do not inform on mating, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, litter sizes, nursing performance and other potential aspects of sexual function and fertility.

2) Toxicity to offspring

Information on pre- and perinatal developmental toxicity reflected by litter sizes, postimplantation loss (resorptions and dead foetuses), stillborns, and external malformations, postnatal developmental toxicity reflected by survival, clinical signs and body weights of the pups (or litters), and other potential aspects related to pre-, peri- and postnatal developmental toxicity observed up to postnatal day 13.

The four studies you submitted provide no information on toxicity to offspring.

3) Systemic toxicity

Information on systemic toxicity include clinical signs, survival, body weights, food consumption, haematology, clinical chemistry, organ weights and histopathology of non-reproductive organs and other potential aspects of systemic toxicity in the parental generation up to postnatal day 13.

The four studies you submitted provide relevant information on systemic toxicity.

Conclusion

Taken together, the sources of information, as indicated above, provide information on reproductive toxicity but essential parts of information of the hazardous property is lacking, including information on: mating, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, litter sizes, nursing performance and other potential aspects of sexual function and fertility; and toxicity to offspring.

Therefore, it is not possible to conclude based on any source of information alone or considered together, whether your Substance has the particular (hazardous) properties. Thus, your adaptation is rejected.

B. Column 2 adaptation

According to Annex VIII, Section 8.7., Column 2, first paragraph, fourth indent, the study does not need to be conducted if a pre-natal developmental toxicity study (OECD TG 414) is already available.

You justified the adaptation by stating that a prenatal developmental toxicity study with the analogue substance cinnamic aldehyde (EC No. 203-213-9) is available and, therefore an EU B.63/OECD TG 421 or EU B.64/OECD TG 422 study does not need to be conducted. However, as explained under section B.1. of this decision the prenatal developmental toxicity study you provided is rejected and it cannot be used to justify an adaptation under Annex VIII, Section 8.7., Column 2, first paragraph, fourth indent. Therefore, your adaptation is rejected.

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

Study design

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[2] administration of the Substance.

Since more severe effects were observed after gavage administration in the OECD TG 407 study ([redacted], 2011) than after dietary administration in an OECD TG 408 study (NTP, 2012) (for instance, significantly liver higher weight observed in males and females at the dose of 300 mg/kg, some behavioural findings, ...), ECHA considers that gavage administration may cause more severe systemic toxicity than dietary administration. Therefore, the study must be conducted using gavage administration.

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

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

1. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study in one species is an information requirement under Annex IX to REACH (Section 8.7.2.).

You have adapted this information requirement by using read-across approach under Annex XI, Section 1.5 with the following supporting information in the dossier:

i) Two automated reports generated from the OECD QSAR Toolbox software with NOAEL values for source substances.

In your comments to the draft decision you indicate that you intend to adapt this information requirement by using another read-across approach under Annex XI, Section 1.5.

We have assessed this information and identified the following issues:

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 source substances . Secondly, it is required that the relevant properties of the Substance may be predicted from data for reference substances.

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

A. Predictions for properties

i) Information provided in the dossier:

You have not provided a read-across justification document in either IUCLID Section 13 or your CSR.

You read across between the following structurally similar substances:

- 4-(2,6,6-trimethylcyclohex-1-en-1-yl)but-3-en-2-one, CAS RN 79-77-6
- 2-hydroxy-4-isopropyl-cyclohepta-2,4,6-trienone, CAS RN 499-44-5
- ethanone, 1-[(3r,3ar,7r,8as)-2,3,4,7,8,8a-hexahydro-3,6,8,8-tetramethyl-1h-3a,7-methanoazulen-5-yl]-acetyl cedrene), CAS RN 32388-55-9

as source substances and the Substance as target substance.

You have not provided any reasoning for the prediction of developmental toxicity properties. However, in support of your read-across, you provided two automated reports generated from the OECD QSAR Toolbox software. On this basis, we understand that the reasoning for the prediction is based on structural similarity, and that you intend to predict the properties of the Substance using a read-across hypothesis which 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 issues with regards to predictions of toxicological properties:

1. Absence of read-across documentation

Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide a justification for the read-across including a hypothesis, explanation of the rationale for the prediction of properties and robust study summary(ies) of the source study(ies).

You have provided two automated reports generated from the OECD QSAR Toolbox software, which do not provide the mandatory information expected in a read-across justification.

In the absence of such documentation, ECHA cannot verify that the properties of your Substance can be predicted from the data on the source substances.

2. *Read-across hypothesis*

A read-across hypothesis needs to be provided, establishing why a prediction for a toxicological or ecotoxicological property is reliable. This hypothesis should be based on recognition of the structural similarities and differences between the source substance(s) and your Substance (ECHA Guidance R.6). It should explain why the differences in the chemical structures should not influence the toxicological/ecotoxicological properties or should do so in a regular pattern.

As already explained above, your hypothesis is based on structural similarity between the Substance and the selected analogue substance. You have selected several analogue substances based on similar outcome of selected profilers from the OECD QSAR Toolbox. However, you have not justified (i) why the profilers you selected are the most relevant and (ii) why the selection of other profilers would not impact the prediction of developmental toxicity properties. Finally, you have not provided any justification on why the structural difference between the Substance and the selected analogues will not impact the prediction. Without this justification, you have not provided a read-across hypothesis establishing why a prediction for a pre-natal developmental property is reliable.

3. *Characterisation of the source substances*

Annex XI, Section 1.5 of the REACH Regulation provides that "*substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as source substance*". According to the ECHA Guidance R.6., "*the purity and impurity profiles of the substance and the structural analogue need to be assessed*", and "*the extent to which differences in the purity and impurities are likely to influence the overall toxicity needs to be addressed, and where technically possible, excluded*". The purity profile and composition can influence the overall toxicity/properties of the Substance and of the selected source substances. Therefore, qualitative and quantitative information on the compositions of the Substance and of the source substances must be provided to allow assessment whether the attempted predictions are compromised by the composition and/or impurities.

You have not provided any information on the composition of the selected analogue substances, including their purity profile and the presence of impurities.

As a result, no qualitative or quantitative comparative assessment of the compositions of the Substance and of the analogue substances can be completed. Therefore, it is not possible to assess whether the attempted predictions are compromised by the composition of the source substances.

4. *Adequacy and reliability of supporting information*

Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable

documentation of the applied method must be provided. Such documentation must provide a justification for the read-across including, among others, robust study summary(ies) of the source study(ies) (ECHA Guidance R.6.2.6.2.). A robust study summary must cover sufficient information to make an independent assessment of the study[3].

To support your predictions, you have provided automated reports generated from the OECD QSAR Toolbox, which only contain NO(A)EL values for category members. Furthermore you stated that the analogue substances produced developmental toxicity effects only at dose levels of maternal toxicity. However you did not provide any justification, or any robust study summaries of the source studies, to establish the validity of this observation.

In the absence of such documentation, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

5. Predictions for no observed (adverse) effect level (NO(A)EL)

Annex XI, Section 1.5. requires that the relevant properties (*i.e.* the key parameters foreseen to be investigated in corresponding test methods) of a substance may be predicted from data on selected analogue substances. When conducting a hazard and risk assessment based on read-across, the results obtained from the studies conducted on the source substances are read across to the target substance. These results form the basis for establishing the no observed (adverse) effect level (NO(A)EL) for the target substance.

However, in order to have a reliable prediction using multiple source substances, the NO(A)EL values need to be based on the same key parameter(s). Furthermore, you must ensure that the read-across prediction is well founded and that the prediction accounts for the uncertainty in the approach. Where there are multiple source substances, and consequently a range of possible values available to read-across, the use of the most conservative (lowest) value may be sufficient to account for the uncertainty in the read-across (ECHA Guidance R.6.2.2.).

You have provided a list of NO(A)EL values for the source substances, and predictions of NO(A)EL values for the Substance, based on the source substances identified with the OECD QSAR Toolbox. You have not provided any information on the key parameter(s) forming the basis to establish the NO(A)EL values. Therefore, we cannot verify that (i) the predicted NO(A)EL is based on the same key parameter(s), (ii) the read-across prediction is well founded and (iii) the prediction accounts for the uncertainty in the approach.

Finally you have not provided adequate justification for the selection of NO(A)EL values of the source substances and therefore an important aspect leading to uncertainty in the approach has not been addressed.

ii) Information provided in the comments to the draft decision:

You have provided a read-across justification document in your comments to the draft decision.

You predict the properties of the Substance from the structurally similar substance: cinnamic aldehyde, EC No. 203-213-9 (CAS No. 104-55-2; i.e. the source substance).

In your read-across approach you refer to two prenatal developmental toxicity studies performed with the source substance: a non-guideline study by [redacted] 1989 and an OECD TG 414 study (2020). However, you do not provide any study records.

[3] How to report robust study summaries Practical Guide 3, Version 2.0 –November 2012

You have provided the following reasoning for the prediction of toxicological properties for the developmental toxicity endpoint:

- *"similarity in chemical structure"*;
- *"physical and chemical properties [...] are in the same range"*;
- *"the toxicokinetic profile [...] is highly similar"*; and
- *"substances have the same toxicological mode of action"*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which 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 shortcomings with regards to the predictions of toxicological properties:

1. *Relevance of the supporting information*

According to the ECHA Guidance[4] *"it is important to provide supporting information to strengthen the rationale for the read-across approach. Thus, in addition to the property/endpoint being read-across, it is also useful to show that additional properties, relevant to the endpoint, are also (qualitatively or quantitatively) similar between the source and target chemicals"*.

In order to support the claim that your Substance and the source substance have similar properties for the endpoints under consideration in the read-across approach, you refer to their acute toxicity, skin irritation and skin sensitisation properties.

Whilst this data set suggests that the substances may have similar properties for acute toxicity, skin irritation, skin sensitisation, these studies do not inform on the developmental and reproductive toxicity properties of the target and source substances. Accordingly, these information are not considered as relevant to support a prediction of the information requirement under consideration.

2. *Missing 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 the source substance.

As indicated above, your read-across hypothesis 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 Substance and of the source substance(s) is necessary to confirm that both substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance.

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

However, you did not submit any relevant bridging studies, such as a screening study for reproductive / developmental toxicity, to demonstrate that the target and source substances may be expected to show similar reproductive / developmental toxicity properties.

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

B. Conclusions on the read-across approach provided in the dossier and in the comments to the draft decision

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substances. Therefore, your adaptations under Annex XI, Section 1.5. are rejected.

On this basis, the information requirement is not fulfilled.

Study design

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

2. Long-term toxicity testing on aquatic invertebrates

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

You have provided QSAR information on long-term toxicity on aquatic invertebrates for the Substance.

For the reasons explained above, in the Appendix entitled "Reasons common to several requests", your adaptation according to Annex XI, Section 1.3 is rejected.

In your comments to the draft decision, you have provided an adaptation to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you argue that: '*As the fish species has shown to be the most sensitive species in short-term studies, the chemical safety assessment according to Annex I does not indicate the need to investigate further effects on aquatic invertebrates.*'

We have assessed this information and identified the following issue:

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

Your adaptation is therefore rejected.

On this basis, the information requirement is not fulfilled.

3. 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 provided QSAR information on long-term toxicity on fish for the Substance.

For the reasons explained above, in the Appendix entitled "Reasons common to several requests", your adaptation according to Annex XI, Section 1.3 is rejected. Therefore, the information requirement is not fulfilled.

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.).

In your comments to the draft decision you agree to perform this study.

Appendix C: 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[6].

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[7].

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

Appendix D: 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 20 March 2020.

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

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

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

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

Appendix E: List of references - ECHA Guidance[8] 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)[9]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[10]

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.

[8] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[9] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[10] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316

OECD Guidance documents[11]
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.

[11] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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

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

Registrant Name	Registration number	(Highest) Data requirements to be fulfilled
[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.