~~Confidential~~

Helsinki, 11 June 2021

**Addressees**
Registrant(s) of CAS527-60-6_JS as listed in the last Appendix of this decision

**Date of submission of the dossier subject to this decision**
13/12/2019

**Registered substance subject to this decision ("the Substance")**
Substance name: 2,4,6-trimethylphenol
EC number: 208-419-2
CAS number: 527-60-6

**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 ***20 June 2022***.

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

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

1. Apply the harmonised classification and labelling on the Substance for mutagenicity or provide reasons for not classifying (Annex VI, Section 4.)

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

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

### C. 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 request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendix entitled "Reasons for the requests to comply with Annex VI of REACH";
- Appendices entitled "Reasons to request information required under Annexes VII and 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 VI, 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 Weight of Evidence adaptation under Annex XI, Section 1.2**

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

- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

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

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

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

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

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

In spite of this critical deficiency, which in itself could lead to the rejection of the adaptation, ECHA has nevertheless assessed the validity of your adaptation.

As your weight of evidence approach has further deficiencies that are specific for these information requirements individually, these are . set out under the information requirement concerned in the Appendix C below.

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

Under Article 10(a) of REACH, a technical dossier must contain information specified in Annex VI to REACH.

1. **Apply the harmonised classification and labelling on the Substance for mutagenicity (Annex VI, Section 4.)**

Classification and labelling of the substance, resulting from the application of Title I, II and III of Regulation (EC) No 1272/2008 (CLP), is an information requirement as specified in Annex VI to REACH.

Your Substance contains [redacted]) as an impurity in its composition to which a harmonised classification applies (Index Number 604-001-00-2).

According to CLP Guidance[2] "*Substances may contain impurities, additives, or other constituents while still meeting the substance definition in CLP. This applies to both mono-constituent, multi-constituent (e.g. reaction masses) and UVCB substances. The classification of such impurities, additives or individual constituents may influence the classification of the substance, in addition to the other hazardous properties. If data on the substance with its components are not available (or for CMRs, see section 1.1.6.1), in principle, the same classification and labelling rules as for mixtures should apply also for such substances".*

Under Article 10(1) of CLP, "*Specific concentration limits and generic concentration limits are limits assigned to a substance indicating a threshold at or above which the presence of that substance in another substance or in a mixture as an identified impurity, additive or individual constituent leads to the classification of the substance or mixture as hazardous*"

Further, according to section 3.5.3.1.1. of Annex I to CLP, a "*mixture shall be classified as a mutagen when at least one ingredient has been classified as a Category 1A, Category 1B or Category 2 mutagen and is present at or above the appropriate generic concentration limit"* triggering classification. This concentration limit is ≥ 1.0 % for Category 2 (Table 3.5.2. of Annex I to CLP).

[redacted] is included in Annex VI to CLP as mutagen, Category 2 (Muta 2) (H341) with a statement "Suspected of causing genetic defects" (harmonised classification).

According to your registration dossier, your Substance is a monoconstituent substance, which contains [redacted] as an impurity in its composition (at a typical concentration of < 0.1% w/w, concentration range > 0 <= 3 % w/w), but you have not classified the Substance as Muta 2, or provided any justification for the non-classification.

Based on the above, you are requested to classify your Substance as Muta 2 or provide reasons for not classifying. These reasons should be scientifically justified.

[2] Guidance on the Application of the CLP Criteria, Section 1.1.7.2

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

### 1. In vitro gene mutation study in bacteria

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

Your dossier does not contain any study or adaptation in accordance with the general rules of Annex XI for this standard information requirement.

*Study design*

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

## Appendix C: 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 (OECD TG 414) in one species is a standard information requirement under Annex IX to REACH.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.2. of REACH (weight of evidence).

In support of your adaptation, you have provided the following study records:

With the Substance:

*(i)* Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (OECD 422, GLP, [redacted], 2007)
*(ii)* Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (OECD 422, GLP, [redacted], 2005).

(Q)SAR predictions (2016):

*(iii)* Danish QSAR database with two models: CASE Ultra (teratogenic potential: negative) and SciQSAR (developmental effects: positive)
*(iv)* Vega platform with two models: Developmental Toxicity model (CAESAR) 2.1.7 (prediction: toxicant) and Developmental/Reproductive Toxicity library (PG) 1.0.0 (prediction: non-toxicant)
*(v)* Leadscope model applier: Retardation foetal growth rat (prediction: negative)
*(vi)* Leadscope model applier: Retardation foetal growth rabbit (prediction:negative)
*(vii)* Leadscope model applier: Foetal weight decrease rat (prediction: negative)
*(viii)* Leadscope model applier: Foetal weight decrease rabbit (prediction: negative)
*(ix)* Leadscope model applier: Foetal death rat (prediction: negative)
*(x)* Leadscope model applier: Foetal death rabbit (prediction: negative)
*(xi)* Leadscope model applier: Post-implantation loss rat (prediction: negative)
*(xii)* Leadscope model applier: Post-implantation loss rabbit (prediction: negative)
*(xiii)* Leadscope model applier: Pre-implantation loss rat (prediction: negative)
*(xiv)* Leadscope model applier: Pre-implantation loss rabbit (prediction: negative)
*(xv)* Leadscope model applier: Structural dysmorphogenesis rat (prediction: negative)

Based on the presented sources of information, you argue that the available data gives sufficient information to conclude on the 1st species prenatal developmental toxicity.

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

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

Based on the information provided, the parameter investigated in the QSAR predictions iii. and iv. and leading to the actual predictions is not specified. In the absence of further information, you have not established which key parameter described above the predictions obtained from the sources of information iii. and iv. relate to. Therefore, based on the information provided, the sources of information iii. and iv. are considered as not providing relevant information and cannot contribute to the conclusion derived from this weight of evidence approach.

As regards the other sources of information they are assessed below.

Prenatal developmental toxicity

Prenatal developmental toxicity includes information after prenatal exposure on embryonic/foetal survivial (number of live foetuses; number of resorptions and dead foetuses, postimplantation loss), growth (body weights and size) and structural malformations and variations (external, visceral and skeletal).

*Embryonic/foetal survival and growth*

The sources of information (i) and (ii) provide relevant information on litter sizes, postnatal survival and growth of pups.
However, they are affected by the following reliability issue:
In order to be considered compliant the set of information provided has to meet the requirements of OECD TG 414. The criteria of this test guideline include that 20 female animals with implantation sites are used for each test and control group.
The studies i. and ii. that you have provided were conducted with 12 and 8 pregnant females for each test group, respectively. The statistical power of the studies i. and ii. provided is not sufficient because it does not fulfil the criterion of 20 pregnant females for each test group set in OECD TG 414.

The QSAR predictions (v.-xv.) provide negative / positive information on some of the elements of pre-natal developmental toxicity such as foetal growth retardation, foetal weight decrease, foetal death, pre- or post-implantation loss. Whilst this information is relevant for the endpoint under consideration, it overlaps with information obtained from *in vivo* studies i. and ii. conducted with the Substance and do not supplement this information. They do not provide information which is not already covered by the experimental studies (i) and (ii). The sources of information v.-xv. do not mitigate the reliability issue identified for the information sources (i) and (ii).

In addition, the (Q)SAR predictions are affected by a reliability issue. Specifically, the uncertainty of the (Q)SAR predictions was assessed as "borderline reliable" for predictions (v-x, xii, xiv) and as "moderate" reliable for predictions (xi, xiii) in the QPRF reports. You justified this assessment by referring to limited structural similarity with analogues included in the training set of the model or inconsistencies between the prediction obtained from the model and the available data on the closest structural analogue in the training set of the model. ECHA agrees with this assessment of the reliability of these sources of information.

Based on the above, the sources of information do not inform reliably on embryonic/foetal survival and growth as foreseen to be investigated in OECD TG 414.

*Embryonic/foetal structural malformations and variations (external, visceral and skeletal)*

The sources of information (i-ii, v-xiv) do not provide information on structural malformations and variations (external, visceral and skeletal) as foreseen to be investigated in the OECD TG

414.

The (Q)SAR prediction (xv.) is the only source of information providing information relevant to embryonic/foetal structural malformations and variations (external, visceral and skeletal). It provides information on structural dysmorphogenesis in rat. However, this QSAR prediction provides a binary positive/negative information, the parameters investigated for the structural dysmorphogenesis are not specified and this QSAR prediction does not inform on the type and incidence of the malformations. In addition, the reliability of this source is affected. Specifically, ECHA agrees with the statement on the uncertainty of the prediction which was assessed as "moderately" reliable in the QPRF report, based on the prediction performance with similar compounds in the training set.
Eventually, as indicated in the ECHA Guidance R.7, Section R.7.6.4.1.2, "*A particular challenge for this endpoint is the complexity and amount of information needed from various functions and parameters to evaluate the effects on reproduction. Not all necessary aspects can be covered by a QSAR prediction. Therefore, a negative result from current QSAR models predicting that the substance has not a particular property, cannot be interpreted as demonstrating the absence of a reproductive hazard unless there is other supporting evidence*". Therefore, this source of information cannot on its own provide the necessary information to embryonic/foetal structural malformations and variations (external, visceral and skeletal) required to comply with this information requirement.

Based on above, the sources of information provided do not inform on structural malformations and variations (external, visceral and skeletal) as foreseen to be investigated in OECD TG 414.

<u>Maternal toxicity</u>

Maternal toxicity includes information after gestational exposure on maternal survival, body weight and clinical signs and other potential aspects of maternal toxicity in dams.

The sources of information (v.-xv.) do not provide relevant information on maternal toxicity.

The sources of information (i) and (ii) provide relevant information on maternal toxicity. However, the reliability of this information is affected by the insufficient number of pregnant females tested, not meeting the requirements of OECD TG 414 as already explained in the section on "Embryonic/foetal survival and growth" above.

Based on above, the sources of information provided do not inform reliably on maternal toxicity as foreseen to be investigated in OECD TG 414.

<u>Maintenance of pregnancy</u>

Maintenance of pregnancy includes information on abortions and/or early delivery as a consequence of gestational exposure and other potential aspects of maintenance of pregnancy.

The sources of information (v.-xv.) do not provide relevant information on maternal toxicity.

The sources of information (i) and (ii) provide relevant information on maintenance of pregnancy. However, the reliability of this information is affected by the insufficient number of pregnant females tested, not meeting the requirements of OECD TG 414 as already explained in the section on "Embryonic/foetal survival and growth" above.

Based on above, the sources of information provided do not inform reliably on maintenance

of pregnancy as foreseen to be investigated in OECD TG 414.

*Conclusion*

For the reasons presented above, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in OECD TG 414, prenatal developmental toxicity study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

*Information on the 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[3] 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 the following information:

i. key study Kuhn *et al*. 1989 (according to guideline "*Provisional Procedure: extended toxicology test with Daphnia magna (determination of NOEC for reproduction rate, mortality and the time of the first aapearance of offspring; 21d)", Federal Environmental Agency, 1 January 1984.*")

We have assessed this information and identified the following issues:

To fulfil the information requirement, a study must comply with the OECD TG 211 (Article 13(3) of REACH). Therefore, the following specifications must be met:

- a reliable analytical method for the quantification of the test material in the test solutions must be available and reported, including reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range;
- the nominal test concentrations and the results of all analyses to determine the concentration of the test substance in the test vessels are reported;
- the test design is reported (*e.g.* semi-static or flow-through, selected test concentrations, number of replicates, number of parents per replicate);
- detailed information on feeding, including amount (in mgC/daphnia/day) and schedule is reported;
- water quality monitoring within the test vessels (*i.e.* pH, temperature and dissolved oxygen concentration) is reported;
- the full record of the daily production of living offspring during the test by each parent animal is provided;
- the number of deaths among the parent animals (if any) and the day on which they occurred is reported;
- the coefficient of variation for control reproductive output is reported;
- the following performance criteria should be met in the control(s):
  - the percentage of mortality of the parent animals (female *Daphnia*) is ≤ 20% at the end of the test;
  - the mean number of living offspring produced per parent animal surviving is ≥ 60 at the end of the test;

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

Your registration dossier provides an OECD TG 211 showing the following:

- on the analytical methods to monitor the test substance concentrations, only the separation method (GC) is reported but no further details on the detector nor performance parameters of the analytical method is provided;
- the nominal test concentrations and the results of all analyses to determine the concentration of the test substance in the test vessels are not reported;
- on the test design, you have not specified selected test concentrations, number of replicates, number of parents per replicate;
- information on feeding rate is not provided;
- water quality monitoring within the test vessels (temperature and dissolved oxygen concentration) are not reported;
- the full record of the daily production of living offspring during the test by each parent animal is not provided;
- the number of deaths among the parent animals (if any) and the day on which they occurred is not reported;
- the coefficient of variation for control reproductive output is not reported;
- it is not specified if performance criteria of the test guideline are met.

Based on the above,

- the reporting of the study does not allow to conduct an independent assessment of the reliability. More specifically, in the absence of information on analytical monitoring, test design and test procedure, and daily production of living offspring and the number of deaths among the parent animals, it is not possible to assess if the study follows OECD TG 211 and would fulfil its validity criteria.

Therefore, the requirements of OECD TG 211 are not met.

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 adapted the standard information requirement mentioned above according to Annex XI, Section 1.2. of REACH (weight of evidence).

In support of your adaptation, you have provided the following sources of information:

(i) Trend analysis from four category members investigating fish, juvenile growth (OECD QSAR Toolbox v.3.4);
(ii) (Q)SAR prediction with "Defined endpoint: FISH ChV" (ECOSAR v.1.11, supported by attached model documetation);
(iii) an experimental study (*Holcombe* et al. 1982) according to guideline equivalent or similar to OECD TG 210, using an analogue substance 2,4-dimethylphenol, EC 203-321-6;

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

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.6 at Annex IX includes similar information that is produced by the OECD TG 210. This includes parameters related to the survival and development of fish in early life stages from the stage of fertilized egg until the juvenile life-stage following exposure to the test substance are measured, including:

1) the stage of embryonic development at the start of the test, and
2) hatching of fertilized eggs and survival of embryos, larvae and juvenile fish, and
3) the appearance and behaviour of larvae and juvenile fish, and
4) the weight and length of fish at the end of the test.

Based on the information provided, all studies (i)-(iii) list only one effect estimate value (NOEC or ChV). For studies (i) and (ii) the "basis of effect", i.e. parameter investigated, is not specified. Study (iii) reports "basis of effect" to be based on growth rate but it is not clear which key parameter listed above this investigation covers. Therefore, you have not demonstrated for any of the sources of information which key parameter described above the provided effect estimate value relates to. Therefore, it cannot be confirmed that the sources of information (i), (ii) and (iii) investigate all or some of the key parameters listed above. Therefore, based on the information provided, they cannot contribute to the conclusion on these key parameters.

Furthermore, the reliability of the sources of information (i) and (iii) is affected by the following deficiencies:

***Reliability of the provided information with analogue substances***

Whenever grouping and read-across is used under REACH, Section 1.5 of Annex XI requires explicitly that "*adequate and reliable documentation of the applied method shall be provided*". According to the ECHA Guidance Section R.6.2.3.1 "*the approach should be documented according to an appropriate format in order to justify that the approach may be used instead of testing. The justification for the read-across should include an explanation of the rationale, as well as the assessment including all relevant supporting information*". The Guidance also specifies the following elements that must be included in the documentation of the adaptation:

1. A read-across hypothesis, establishing why a prediction for a toxicological or ecotoxicological property is reliable;
2. Scientific information substantiating that the prediction of the properties is justified for each relevant endpoint, taking into account the structural differences between the substances;
3. Robust study summaries of the source studies.

We have assessed the information provided in your technical dossier and identified the following issues:

1. "*Adequate and reliable documentation of the applied method*" in the form of a read-across hypothesis establishing why a prediction of property is reliable

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

In your read-across justification you state that:

- For the analogue approach (source iii): *"The hypothesis of this analogue approach is based on common functional groups (the target substance and the source substance are both* [redacted] *under "US-EPA New Chemical Categories"), and based on additional subcategorization on common end-point specific profiling (based on "Aquatic toxicity classification by ECOSAR") and high structural similarity (60-70% based on Dice (Atom centered fragment))."*
- For the category approach (source i): You do not formulate a clear hypothesis but provide an OECD QSAR Toolbox report which provides the structural and mechanistic basis how the source substances were selected;

We understand that the hypothesis for both of the predictions is that the structural similarity is a sufficient basis for predicting the properties of the Substance.

While structural similarity is a prerequisite for applying the grouping and read-across approach, it does not necessarily lead to predictable or similar human health and ecotoxicological properties in other endpoints. As described above, a well-founded hypothesis is needed to establish a reliable prediction for a toxicological or ecotoxicological property, based on recognition of the structural similarities and differences between the source substance(s) and your Substance.

2. "*Adequate and reliable documentation of the applied method*" in the form of scientific information substantiating that the prediction of the properties is justified for each relevant endpoint

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. 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*"." (ECHA Guidance R.6, Section R.6.2.2.1.f). The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include relevant and reliable information (experimental studies or reliable predictions) to support the claimed similarity in physico-chemical, ecotoxicological and toxicological properties of the Substance and source substances. Variations in chemical structure can affect both toxicokinetics (uptake and bioavailability) and toxicodynamics (e.g. interactions with receptors and enzymes). Therefore the information provided to support the predictions must explain why the differences in the chemical structures should not influence their toxicological, ecotoxicological and fate properties or should do so in a regular pattern (ECHA Guidance R.6., Section 6.2.1.).

The technical dossier does not include any data for the Substance which would investigate the properties under consideration (survival and development of fish in early life stages). There is also no other aquatic toxicity data provided for the source substances - apart from those used in this Weight of evidence approach (sources i and iii) – allowing to compare aquatic toxicity for your Substance and the source substances, e.g. bridging studies of comparable design and duration.

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

3. "*Adequate and reliable documentation of the applied method*" in the form of a robust study summary of each source study

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*". When properties of a substance are read-across from a source study conducted with an analogue substance to fulfil an information requirement, this source study provides key data for the hazard assessment. Therefore a robust study summary providing information allowing to make an independent assessment of the study must be provided for each source study used in read-across approaches.

Robust study summary must provide a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study (Article 3(28)).

In the category approach (source iii), you have provided a justification document where you have identified the studies conducted with analogue substances that you intend to use as source studies in your read-across approach. You have not provided robust study summaries for any for these source studies.

In the analogue approach (source i), you have provided a robust study summary for the source study that you intend to use in your read-across approach. In this robust study summary you report only the test species, test substance and one effect estimate (for growth rate).

While for the category approach you provided no robust study summaries at all, for the analogue approach you have not provided detailed information on the methods, results and conclusions of these studies allowing for an independent assessment of the study. In the absence of such information, we cannot assess the reliability of the information used to predict the properties of the Substance.

**Conclusion**

For all the reasons presented above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substances. This information cannot contribte to deriving reliable conclusions on the properties of the Substance in a weight of evidence approach.

***Conclusions on the Weight of evidence approach***

Taken together, you have not demonstrated that the sources of information cover the key investigations as indicated above and they are also affected by issues in reliability. Furthermore, you did not provide any documentation for assessment of the relative values/weights of the different sources of information.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 210 study.

Therefore, your adaptation is rejected and the information requirement is not fulfilled.

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

### A. Test methods, GLP requirements and reporting

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

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

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

### B. Test material

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 technical grade boundary composition(s) of the Substance. This composition includes minor constituents and impurities which may affect the toxicological properties of the Substance. The impact of exposure to all the constituents and impurities of the Substance needs to be accounted for in the generation of the new data.

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.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[5].

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

**Appendix E: 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 28 July 2020.

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

ECHA did not receive any comments within the notification period.

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

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

**Appendix F: List of references - ECHA Guidance[6] 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)[7]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[7]

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

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

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

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

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

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

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

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

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

OECD Guidance documents[8]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

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

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

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

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

**Appendix G: 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 REACH Annex applicable to you |
|---|---|---|
| [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.