~~Confidential~~

Helsinki, 16 June 2023

Addressee
Registrant of JS_22374-89-6_[redacted] as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
14/03/2018

Registered substance subject to this decision ("the Substance")
Substance name: 1-methyl-3-phenylpropylamine
EC number/List number: 244-942-2

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 ***24 June 2024***.

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

Information required from 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: OECD TG 471, 2020)

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

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

The reasons for the requests are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

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 requirements for testing and reporting new tests under REACH, see Appendix 4.

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 Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the request(s)
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 1: Reasons for the request(s)

Contents

Reasons common to several requests

0.1. Weight of evidence adaptation rejected

1 You have adapted the following standard information requirements by using Annex XI, Section 1.2. (weight of evidence):

- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- In vitro gene mutation in bacteria (Annex VII, section 8.4.1)

2 Annex XI, Section 1.2. states that there may be sufficient weight of evidence from several independent sources of information enabling, through a reasoned justification, a conclusion on the information requirement, while the information from each single source alone is insufficient to fulfil the information requirement.

3 The justification must have regard to the information that would otherwise be obtained from the study that must normally be performed for this information requirement.

4 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 on the corresponding information requirement.

5 Your weight of evidence approach has deficiencies that are common to all information requirements under consideration and also deficiencies that are specific for these information requirements individually.

6 The common deficiencies are set out here, while the specific ones are set out under the information requirement concerned in request(s) 1,2, and 3 below.

0.1.1. Lack of documentation justifying the weight of evidence adaptation

7 Annex XI, Section 1.2. requires that adequate and reliable documentation is provided to describe a weight of evidence approach. This documentation must include robust study summaries of the studies used as sources of information and a justification explaining why the sources of information together provide a conclusion on the information requirement.

8 You have not included a justification for your weight of evidence adaptation for each of the relevant information requirement, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude on the information requirements under consideration.

0.1.2. Only one source of information provided (for Requests 2 and 3)

9 Annex XI, Section 1.2. states that there may be sufficient weight of evidence from several independent sources of information based on which a conclusion on the information requirement can be drawn.

10 For the endpoints short term toxicity on aquatic invertebrates and growth inhibition on aquatic plants/ algae, you have only provided one source of information (i.e. an adaptation under Annex XI, Section 1.5).

11 Therefore, your weight of evidence adaptation does not rely on several independent sources of information as required by Annex XI, Section 1.2. Furthermore, for the reasons explained

under Section 0.2., the provided read-across adaptations suffer from major reliability issues and therefore cannot contribute to a weight of evidence for the information requirements listed above

0.1.3. Conclusion on the weight of evidence approaches

12 For the reasons explained above, it is not possible to conclude, based on the information you provided, whether the Substance has or has not the particular dangerous properties foreseen to be investigated by the information requirements listed above. Your read-across approaches under Annex XI, Section 1.2. are rejected.

0.2. Read-across adaptation rejected

13 You have adapted the following standard information requirements by using grouping and read-across approach under Annex XI, Section 1.5:

- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- In vitro gene mutation in bacteria (Annex VII, section 8.4.1)

14 ECHA has considered the scientific and regulatory validity of your read-across approaches in general before assessing the specific standard information requirements in the following sections.

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

16 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

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

0.2.1. Scope of the grouping of substances – identification of source substances

18 You predict the properties of the Substance from information obtained from the following source substance(s):

- benzyl 3-methylbutanoate, EC number 203-106-7 (source substance 1);
- benzyl 2-methylpropanoate, EC number 203-095-9 (source substance 2);
- benzyl butyrate, EC number 203-105-1 (source substance 3)
- [redacted] (source substance 4).

19 You have provided no reasoning for the prediction of (eco)toxicological properties.

20 ECHA assumes that your read-across hypothesis assumes that different compounds have the same type of effects. ECHA also assumes that you predict the properties of your Substance to be quantitatively equal to those of the source substance.

0.2.2. Predictions for (eco)toxicological properties

0.2.2.1. Absence of read-across documentation

21 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 include

an explanation why the properties of the Substance may be predicted from information on the source substances.

22 You have provided robust study summaries for the studies conducted with other substances than the Substance in order to comply with the REACH information requirements. However, you have not provided documentation to explain why this information is relevant for the Substance and why the properties of the Substance may be predicted from information on the source substances.

23 In the absence of such documentation, the properties of the Substance cannot be reliably predicted from the data on the source substances.

0.2.2.2. Missing supporting information to compare the properties of the substances

24 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 supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substances (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).

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

26 For the selected source substances, you provide the studies used in the prediction in the registration dossier. Apart from these studies, your registration dossier does not include any robust study summaries or descriptions of data for the Substance that would confirm that both substances cause the same type of effects.

27 In addition, specific reasons why the provided studies on the selected analogue substances cannot be considered reliable are explained further below under the relevant information requirement sections 1,2 and 3.Thus the data set reported in the technical dossier does not include relevant, reliable and adequate information for the source substances to support your read-across hypothesis.

28 In the absence of such information, you have not established that the Substance and the source substances are likely to have similar properties. Therefore you have not provided sufficient supporting information to scientifically justify the read-across.

0.2.3. Conclusion on the read-across approaches

29 For the reasons explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substances. Your read-across approaches under Annex XI, Section 1.5. are rejected.

Reasons related to the information under Annex VII of REACH

1. In vitro gene mutation study in bacteria

30 An in vitro gene mutation study in bacteria is an information requirement under Annex VII, Section 8.4.1.

1.1. Information provided

31 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on the following experimental data and prediction:

(i) an *in vitro* gene mutation study in bacteria (1986) with the source substance [redacted]

(ii) an *in vitro* gene mutation study in bacteria (2002) with the Substance;

(iii) a prediction from Danish QSAR Database 2018.

1.2. Assessment of the information provided

1.2.1. Weight of evidence adaptation rejected

32 As explained in Section 0.1., your adaptation based on weight of evidence under Annex XI, Section 1.2. is rejected. In addition, ECHA identified endpoint specific issue(s) addressed below.

33 Relevant information that can be used to support weight of evidence adaptation for the information requirement of Annex VII, Section 8.4.1. includes similar information that is produced by the OECD TG 471 with a design as specified in this decision. OECD TG 471 requires the study to investigate the following key element:

(1) detection and quantification of gene mutation (base pairs, substitution or frameshift) in cultured bacteria including data on the number of revertant colonies.

34 The sources of information ((i)-(ii)) may provide relevant information on the above mentioned key parameter.

35 However, the reliability of these sources of information is significantly affected by the following deficiency/deficiencies:

1.2.1.1. Source of information (i): Read-across rejected

36 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected. In addition, ECHA has identified the endpoint specific issues listed below.

1.2.1.1.1. The provided study does not meet the specifications of the test guideline(s)

37 To inform on in vitro gene muta in bacteria in the context of the weight-of-evidence adaptation, a study must normally be conducted under conditions that are consistent with the specifications of the OECD TG 471. Therefore, the following specifications must be met:

a) the test is performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

the source of information (i) was performed with the strains TA 1535, TA 1537, TA 98,TA 97 and TA 100 (i.e., the strain TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101) missing);

b) the maximum dose tested induces a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose corresponds to 5 mg/plate or 5 µl/plate;

the source of information (i) does not indicate if the maximum dose tested induces a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance and it was less than 5 mg/plate or 5 µl/plate;

c) at least 5 doses are evaluated, in each test condition;

the source of information (i) evaluated only 4 doses.

d) triplicate plating is used at each dose level;

the source of information (i) does not indicate if triplicate plating was used.

e) concurrent strain-specific positive controls, both with and without metabolic activation, are included in each assay and the number of revertant colonies per plate induced by the positive controls demonstrates the effective performance of the assay;

the number of revertant colonies per plate is not provided and therefore the effective performance of the assay cannot be demonstrated

f) a concurrent negative control is included in each assay and the number of revertant colonies per plate for the concurrent negative control is inside the historical control range of the laboratory;

the source of information (i) does not provide the number of revertant colonies per plate nor the historical control range.

g) the mean number of revertant colonies per plate is reported for the treated doses and the controls;

the source of information (i) does not provide the mean number of revertant colonies per plate for the treated doses and the controls was not reported;

h) negative results are confirmed in a repeat experiment with modification of study parameters to extend the range of conditions assessed, or a justification why confirmation of negative results is not considered necessary is provided.

No repeat experiment was performed in the sources of information (i) to confirm the negative results nor a justification was provided

38 On this basis, the information provided does not cover the specifications required by the OECD TG 471.

39 Therefore the provided study cannot be considered a reliable source of information that could contribute to the conclusion on this key parameter investigated by the required study.

1.2.1.2. Source of information (ii): the provided study does not meet the specifications of the test guideline(s)

40 To inform on in vitro gene muta in bacteria in the context of the WoE adaptation, a study must normally be conducted under conditions that are consistent with the specifications of the OECD TG 471. Therefore, the following specifications must be met:

a) the maximum dose tested induces a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose corresponds to 5 mg/plate or 5 µl/plate;

the source of information (ii) does not indicate if the maximum dose tested induces a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance and it was less than 5 mg/plate or 5 µl/plate;

b) triplicate plating is used at each dose level;

the source of information (ii) does not indicate if triplicate plating was used.

c) concurrent strain-specific positive controls, both with and without metabolic activation, are included in each assay and the number of revertant colonies per plate induced by the positive controls demonstrates the effective performance of the assay;

the number of revertant colonies per plate is not provided and therefore the effective performance of the assay cannot be demonstrated

d) a concurrent negative control is included in each assay and the number of revertant colonies per plate for the concurrent negative control is inside the historical control range of the laboratory;

the source of information (ii) does not provide the number of revertant colonies per plate nor the historical control range.

e) the mean number of revertant colonies per plate is reported for the treated doses and the controls;

the source of information (ii) does not provide the mean number of revertant colonies per plate for the treated doses and the controls was not reported;

f) negative results are confirmed in a repeat experiment with modification of study parameters to extend the range of conditions assessed, or a justification why confirmation of negative results is not considered necessary is provided.

No repeat experiment was performed in the sources of information (ii) to confirm the negative results nor a justification was provided

41 On this basis, the information provided does not cover the specifications required by the OECD TG 471.

42 Therefore the provided study cannot be considered a reliable source of information that could contribute to the conclusion on this key parameter investigated by the required study.

1.2.1.3. Source of information (iii): (Q)SAR adaptation rejected

1.2.1.3.1. The QSAR result is not equivalent to results obtained from the required experimental test

43 Results from (Q)SAR models are adequate for risk assessment or classification and labelling when they are equivalent to results obtained from the required experimental test. The

corresponding study that must normally be performed for this particular information requirement is OECD TG 471, which measure(s): in vitro gene mutation in bacteria.

44 You have provided the prediction from a (Q)SAR model (i.e., Danish QSAR database) which predicts in vitro gene mutation study in bacteria.

45 The model predicts in vitro gene mutation study in bacteria but does not measure systematically the 5 strains. Therefore, the prediction is not adequate to meet the information requirement for in vitro gene mutation study in bacteria for the purpose of classification and labelling and/or risk assessment.

1.2.1.3.2. Lack of documentation of the prediction (QPRF)

46 ECHA Guidance R.6.1.6.3. states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:

- the relationship between the modelled substance and the defined applicability domain;
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

47 You have provided a "negative" prediction for the Substance without further details on the relationship between the modelled substance and the defined applicability domain and the identity of close analogues.

48 In absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.

49 Based on the above, your QSAR adaptation under Annex XI, Section 1.3. is rejected.

50 Therefore the provided prediction from (Q)SAR models cannot be considered a reliable source of information that could contribute to the conclusion on this key parameter investigated by the required study.

1.2.1.4. Conclusion on the weight-of-evidence

51 In summary, the sources of information (i) to (iii) provide limited relevant information on detection and quantification of gene mutation. However, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for in vitro gene mutation study in bacteria.

52 It is not possible to conclude, based on any source of information alone or considered together, on the information requirement for in vitro gene mutation study in bacteria.

53 Based on the above, your adaptation is rejected.

54 Therefore, the information requirement is not fulfilled.

55 In your comments to the draft decision, you agree to perform the requested study.

1.3. Specification of the study design

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

2. Short-term toxicity testing on aquatic invertebrates

57 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

2.1. Information provided in your dossier

58 You have adapted this standard information requirement according to Annex XI, Section 1.2. of REACH (weight of evidence). In support of your adaptation, you have provided the following source of information:

(1) a short-term toxicity study on aquatic invertebrates according to OECD TG 202 (2017) with the analogue substance benzyl 3-methylbutanoate (EC number 203-106-7)

(2) a short-term toxicity study on aquatic invertebrates according to OECD TG 202 (2017) with the analogue substance benzyl 2-methylpropanoate (EC number 203-095-9)

(3) a short-term toxicity study on aquatic invertebrates according to OECD TG 202 (2017) with the analogue substance benzyl butyrate (EC number 203-105-1)

2.2. Assessment of the information provided in your dossier

2.2.1. The weight of evidence adaptation is rejected

59 As explained in Section 0.1., your adaptation based on weight of evidence under Annex XI, Section 1.2. is rejected. In addition, ECHA identified endpoint specific issues addressed below.

60 Relevant information that can be used to support weight of evidence adaptation for the information requirement of Annex VII, Section 9.1.1. includes similar information that is produced by the OECD TG 202 with a design as specified in this decision. OECD TG 202 requires the study to investigate the following key element:

- the concentration of the test material leading to the immobilisation of 50% of daphnids at the end of the test (i.e. at least 48h) is estimated.

61 The source of information (i) may provide relevant information on the above key element.

62 However, in addition to the common issues detailed under Section 0.1., the reliability of this source of information is significantly affected by the following deficiencies:

2.2.1.1. Read-across adaptation rejected

63 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected. In addition, ECHA has identified the endpoint specific issues listed below.

2.2.1.1.1. Unclear test material identity

64 To comply with this information requirement, the test material in a study must be representative for the selected analogue substance; Article 10 and Recital 19 of REACH; Guidance on IRs and CSA, Section R.4.1.

65 For the studies (1) to (3), you have provided no information on purity and on composition.

66 In the absence of purity and composition information on the test materials, the identity of the test materials and their impurities cannot be assessed, and you have not demonstrated that the test materials were representative for the selected analogue substances.

2.2.1.1.2. The provided studies do not meet the specifications of the test guideline

67 To fulfil the information requirement, a study must comply with OECD TG 202 and the specification(s) of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Characterisation of exposure

a) analytical monitoring must be conducted. A reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;

Reporting of the methodology and results

b) the test procedure is reported (*e.g.* composition of the test medium);

c) the number of immobilised daphnids is determined at 24 and 48 hours. Data are summarised in tabular form, showing for each treatment group and control, the number of daphnids used, and immobilisation at each observation.

68 In studies (1) to (3):

Characterisation of exposure

a) no analytical monitoring of exposure is reported

69 Reporting of the methodology and results

b) on the test procedure, you have not specified the nature and composition of the dilution water(including its content in TOC/DOC);

c) tabulated data on the number of immobilised daphnids after 24 and 48 hours for each treatment group and control are not reported.

70 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the provided studies. More specifically, in the absence of analytical verification of exposure concentrations, you have not demonstrated that test organisms were satisfactorily exposed to the test material over the exposure period.
- the reporting of the studies is not sufficient to conduct an independent assessment of their reliability. More specifically, you have not provided adequate information on the test medium to assess whether it complies with the requirements of the test guideline. Furthermore, in the absence of tabulated data on the number of immobilised daphnids, ECHA cannot conduct an independent assessment of the interpretation of the results of these studies.

71 On this basis, the specifications of the OECD TG 202 are not met by any of the provided studies.

72 For the reasons explained above, the weight of evidence adaptation is rejected and the information requirement is not fulfilled.

2.3. Information provided in your comments on the draft decision

73 In your comments on the draft decision, you provide a robust study summary for a new OECD TG 202 study (no reference provided; [redacted]) conducted on the Substance in order to replace the incompliant weight of evidence adaptation evaluated above.

2.1. Assessment of the information provided in your comments on the draft decision

74 ECHA has assessed the new information provided in your comments and concludes that it could address the information requirement. However, as the information is currently not available in your registration dossier, the data gap remains. You should submit this information in an updated registration dossier by the deadline set in the decision.

2.2. Study design and test specifications

75 The Substance is difficult to test due to its ionisable properties (i.e. positively charge under environmentally relevant pH) and surface active properties (surface tension of 27 mN/m). OECD TG 202 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

3. Growth inhibition study aquatic plants

76 Growth inhibition study on aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

3.1. Information provided in your dossier

77 You have adapted this standard information requirement according to Annex XI, Section 1.2. of REACH (weight of evidence). In support of your adaptation, you have provided the following source of information:

(1) a growth inhibition study on aquatic plants/algae according to OECD TG 201 (2015) with the analogue substance benzyl butyrate (EC number 203-105-1)

(2) a growth inhibition study on aquatic plants/algae according to OECD TG 201 (2017) with the analogue substance benzyl 2-methylpropanoate (EC number 203-095-9)

(3) a growth inhibition study on aquatic plants/algae according to OECD TG 201 (2016) with the analogue substance benzyl 3-methylbutanoate (EC number 203-106-7)

3.2. Assessment of the information provided in your dossier

3.2.1. The weight of evidence adaptation is rejected

78 As explained in Section 0.1., your adaptation based on weight of evidence under Annex XI, Section 1.2. is rejected. In addition, ECHA identified endpoint specific issues addressed below.

79 Relevant information that can be used to support weight of evidence adaptation for the information requirement of Annex VII, Section 9.1.1. includes similar information that is

produced by the OECD TG 202 with a design as specified in this decision. OECD TG 202 requires the study to investigate the following key element:

- the concentration of the test material leading to the immobilisation of 50% of daphnids at the end of the test (i.e. at least 48h) is estimated.

80 The source of information (i) may provide relevant information on the above key element.

81 However, in addition to the common issues detailed under Section 0.1., the reliability of this source of information is significantly affected by the following deficiencies:

3.2.1.1. Read-across adaptation rejected

82 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected. In addition, ECHA has identified the endpoint specific issues listed below.

3.2.1.1.1. Unclear test material identity

83 To comply with this information requirement, the test material in a study must be representative for the selected analogue substance; Article 10 and Recital 19 of REACH; Guidance on IRs and CSA, Section R.4.1.

84 For the studies (1) to (3), you have provided no information on purity and on composition.

85 In the absence of purity and composition information on the test materials, the identity of the test materials and their impurities cannot be assessed, and you have not demonstrated that the test materials were representative for the selected analogue substances.

3.2.1.1.2. The provided studies do not meet the specifications of the test guideline

86 To fulfil the information requirement, a study must comply with OECD TG 201 and the specification(s) of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Validity criteria

a) the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%;

Characterisation of exposure

b) analytical monitoring must be conducted. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;

87 Reporting of the methodology and results

c) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

88 In studies (1) to (3):

Validity criteria

a) for study (1), the mean coefficient of variation for section-by-section specific growth in the control was 137%;

Characterisation of exposure

b) no analytical monitoring of exposure is reported for study (1). For studies (2) and (3), you specify that no analytical monitoring was conducted;

89 Reporting of the methodology and results

c) for studies(2) and (3), tabulated data on the algal biomass determined daily for each treatment group and control are not reported.

90 Based on the above,

- the validity criteria of OECD TG 201 are not met for study (1)
- there are critical methodological deficiencies resulting in the rejection of the provided studies (1) to (3). More specifically, in the absence of analytical verification of exposure concentrations, you have not demonstrated that test organisms were satisfactorily exposed to the test material over the exposure period.
- the reporting of the studies (2) and (3) is not sufficient to conduct an independent assessment of their reliability. More specifically, as you have not provided tabulated data on the algal biomass, ECHA cannot conduct an independent assessment as to whether the validity criteria of the test guideline were met and of the interpretation of the results of these studies.

91 On this basis, the specifications of the OECD TG 201 are not met by any of the provided studies.

92 For the reasons explained above, the weight of evidence adaptation is rejected and the information requirement is not fulfilled.

3.3. Information provided in your comments on the draft decision

93 In your comments on the draft decision, you provide a robust study summary for a new OECD TG 201 study (no reference provided; [redacted]) conducted on the Substance in order to replace the incompliant weight of evidence adaptation evaluated above.

3.4. Assessment of the information provided in your comments on the draft decision

3.4.1. The information provided on the study is not sufficient to conduct an independent assessment of its reliability

94 To fulfil the information requirement, a study must comply with OECD TG 201 and the specification(s) of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specification(s) must be met:

Characterisation of exposure

a) the test media prepared specifically for analysis of exposure concentrations during the test is treated identically to those used for testing (*i.e.* inoculated with algae and incubated under identical conditions).

95 In the new study provided in your comments on the draft decisions:

Characterisation of exposure

a) You have not specified whether the test media prepared specifically for analysis of exposure concentrations during the test were inoculated with algae and incubated under identical conditions.

96 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, you have not described how the test media used for the analysis of exposure concentrations were prepared. Therefore, it is unclear whether the reported values reflect true exposure during the test. ECHA notes that after an initial marked growth inhibition in the first 48h hours of the test, a reduction in effects was

observed at 48h-72h in all tested concentrations (with growth rates at or above that of the controls). As specified in paragraph 40 of the OECD TG 201, if a decrease in measured concentrations is observed and is accompanied by a decrease in growth inhibition, a suitable model describing the decline of the concentration of the test material must be used.

97 ECHA has assessed the new information provided in your comments and concludes that it could address the information requirement providing that you can clarify the deficiency identified above. However, as the information is currently not available in your registration dossier, the data gap remains. You should submit this information in an updated registration dossier by the deadline set in the decision.

3.5. Study design and test specifications

98 OECD TG 201 that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design and test specifications" under request 2.

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).
Guidance for monomers and polymers; ECHA (2012).
Guidance on intermediates; ECHA (2010).
All guidance documents are available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF); ECHA (2017).
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs; ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: 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 14 June 2022.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 6 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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

ECHA took into account your comments and did not amend the requests.

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 3: Addressee(s) of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- 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;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

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.

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. 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[2].

(4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2. 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.

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

- The reported composition must include all constituents of each Test Material and their concentration values

With that detailed information, ECHA can confirm 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 (https://echa.europa.eu/manuals).

References to Guidance on REACH and other supporting documents can be found in Appendix 1.