~~Confidential~~

Helsinki, 22 August 2022

Addressees
Registrant(s) of JS_3358-60-9_[redacted] as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
06/10/2021

Registered substance subject to this decision ("the Substance")
Substance name: (2-methoxyethyl)benzene
EC number: 222-619-7

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 ***27 November 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. Vapour pressure (Annex VII, Section 7.5.; test method: EU A.4./OECD TG 104)

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

3. Skin sensitisation (Annex VII, Section 8.3.; test method:
   i. *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (EU B.71/OECD TG 442E)(Annex VII, Section 8.3.1.); and
   ii. Only if the *in vitro/in chemico* test methods specified under point 3.i. are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429);

4. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: OECD TG 471, 2020)

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

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

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

7. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)

8. If negative results are obtained in tests performed for the information requirement of Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

9. Short-term repeated dose toxicity (28 days; Annex VIII, Section 8.6.1.) to be combined with the Screening for reproductive/developmental toxicity below

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

    A combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test (2018), is available in the opt-out registrant's submitted registration for the Substance (Registration No. [redacted]). Under Article 26(3) of REACH, you must not repeat a study involving vertebrate animals conducted on the Substance.

11. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: EU C.1./OECD TG 203)

    A fish, acute toxicity test (2018), is available in the opt-out registrant's submitted registration for the Substance (Registration No. [redacted]). Under Article 26(3) of REACH, you must not repeat a study involving vertebrate animals conducted on the Substance.

The reasons for the decision(s) 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 decision
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 decision

Contents

0. Reasons common to several requests

0.1. Assessment of weight of evidence adaptations

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

- Skin sensitisation (Annex VII, Section 8.3)
- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

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

3 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.

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 information requirement.

5 Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach. This documentation must include a justification explaining why the sources of information together provide a conclusion on the information requirement.

6 You have provided summaries in separate endpoint study records for skin sensitisation, genotoxicity, reproductive toxicity and all three aquatic toxicity endpoints listed above. In those summaries you briefly present each of the sources of information, describe the results and conclude that this information can be used as weight of evidence to predict the (eco)toxicological properties of the Substance for the above-mentioned endpoints.

7 Whilst these reports can be regarded as integrated summaries of the data sets, you have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to a conclusion on the information requirement.

8 In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation and identified the following issues.

9 Your weight of evidence adaptation has deficiencies that are common to all information requirements under consideration and also deficiencies that are specific for these information requirements individually. The common deficiencies are set out here, while the specific ones are set out under the information requirement concerned in the Appendices below.

0.1.1. Reliability of the provided information with analogue substances and Assessment of the read-across approach

10 ECHA understands that you intend to predict the (eco)toxicological properties of the Substance for the above listed endpoints, from data obtained with analogue substances in a read-across approach as part of your weight of evidence adaptation.

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

12 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.

13 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).

0.1.2. Predictions for (eco)toxicological properties

14 You have not provided a read-across justification document.

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

[1] 1-Hydroxy-2-phenoxyethane, EC No. 204-589-7
[2] 2-Methoxybenzyl alcohol, EC No. 210-296-5
[3] Methyl benzoate, EC No. 202-259-7
[4] 1-Phenylethanol, EC No. 202-707-1
[5] Ethylbenzene, EC No. 202-849-4
[6] 2-Methoxynaphthalene, EC No. 202-213-6
[7] 2-Phenylethyl phenylacetate, EC No. 203-013-1
[8] Benzyl propionate, EC No. 204-559-3
[9] 1-Methoxy-4-methylbenzene, EC No. 203-253-7
[10] Benzyl alcohol, EC No. 202-859-9
[11] 2-Phenylethanol, EC No. 200-456-2
[12] Methoxybenzene, EC No. 202-876-1

16 In absence of any justification document, ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

17 We have identified the following issue(s) with the prediction(s) of (eco-)toxicological properties:

0.1.2.1. Absence of read-across documentation

18 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

an explanation why the properties of the registered substance may be predicted from other substances in the group including a hypothesis, explanation of the rationale for the prediction of properties and robust study summary(ies) of the study(ies) on the source substance(s) (Guidance on IRs and CSA, Section R.6.2.6.1.).

19 You have provided robust study summaries for studies conducted with other substances than the Substance in order to comply with the REACH information requirements. However, you have not provided documentation as to why this information is relevant for the Substance.

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

0.1.2.2. Missing supporting information to compare properties of the substances

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 provide supporting information to scientifically justify the read-across explanation for prediction of properties. 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) (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).

22 Supporting information must include bridging studies to compare properties of the Substance and source substances.

23 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(s).

24 You have provided a repeated dose toxicity study and short-term toxicity to fish study with the Substance as supporting information. Apart from these studies, your read-across justification or the 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 investigated under standard information requirements listed above.

25 The repeated-dose toxicity study provided for the Substance is rejected as explained in the endpoint section. Furthermore, the data on repeated dose toxicity only gives limited information for the screening for reproductive toxicity endpoint. For genotoxicity and skin sensation no information on the Substance is available.

26 Furthermore, short-term toxicity to fish study provided for the Substance is rejected as explained in the endpoint section. For short-term toxicity to aquatic invertebrates and algal toxicity no information on the Substance is available.

27 In the absence of such information, you have not established that the Substance and 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.

0.1.3. Conclusion on the read-across approach

28 For the reasons above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approach (as under Annex XI, Section 1.5.) is rejected.

0.2. Assessment of (Q)SAR information

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

- Vapour pressure (Annex VII, Section 7.5.)
- Surface tension (Annex VII, Section 7.6.)

30 ECHA has considered the scientific and regulatory validity of your (Q)SAR adaptation(s) in general before assessing the specific standard information requirements in the following appendices.

31 Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

(1) the prediction needs to be derived from a scientifically valid model,

(2) the substance must fall within the applicability domain of the model,

(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.

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

33 Under Appendix C of the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) and ECHA Guidance R.6.1.6.3., adequate and reliable documentation must include a (Q)SAR Model Reporting Format document (QMRF) which reports, among others, the following information:

- the predicted endpoint, including information on experimental protocol and data quality for the data used to develop the model;
- an unambiguous definition of the algorithm, the descriptor(s) of the model and its applicability domain,
- an estimate of the goodness-of-fit and of the predictivity of the model, including information on training set and validation statistics.

34 Furthermore, 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 model prediction(s), including the endpoint,
- a precise identification of the substance modelled,
- 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.

35 You have not provided information about the models and predictions for neither vapour pressure nor surface tension.

36 Furthermore, it should be noted that, as explained in the ECHA Guidance R.7a (section 7.1.6) and OECD TG 115, the property investigated (measured) under standard information

requirement for Surface tension (Annex VII, Section 7.6.) is "surface tension measurements of aqueous solution", i.e. "Measurements should be performed on a solution at either 90 % of the solubility limit or 1 g/l (where viscosity permits), whichever is smaller.". Therefore, predicted endpoint for the surface tension must be "surface tension measurements of aqueous solution" of the Substance.

37 In absence of such information, ECHA cannot establish that the models and the predictions can be used to meet these information requirements.

38 Based on the above, your adaptation is rejected.

Reasons related to the information under Annex VII of REACH

1. Vapour pressure

39 Vapour pressure is a standard information requirement in Annex VII to REACH (Section 7.5.).

1.1. Information provided

40 You have provided an adaptation under Annex XI, Section 1.3. ('(Q)SAR'). In support of your adaptation, you provide the following information: a prediction derived from "Estimation Programs Interface Suite™ United States Environmental Protection Agency, Washington, DC, USA. version 4.1" using (2-methoxyethyl)benzene (EC No 222-619-7) as an input structure.

1.2. Assessment of the information provided

41 We have assessed this information and identified the following issue. As explained under section 0.2 above, your adaptation is rejected.

42 Based on the above, your adaptation is rejected.

43 On this basis, the information requirement is not fulfilled.

1.3. Information regarding data sharing

44 The opt-out registrant's registration for the Substance (Registration No. [redacted]) contains a study on vapour pressure (2019) which is adequate for this information requirement. In accordance with Title III of the REACH Regulation, you may request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing).

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

2. Surface tension

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

2.1. Information provided

47 You have provided an adaptation under Annex XI, Section 1.3. ('(Q)SAR'). In support of your adaptation, you provide the following information: a prediction derived from "ACD lab Algorithm Version: v12.1.0.50375" using (2-methoxyethyl)benzene (EC No 222-619-7) as an input structure.

2.2. Assessment of the information provided

48 We have assessed this information and identified the following issue:

49 As explained under section 0.2 above, your adaptation is rejected.

50 Based on the above, your adaptation is rejected.

51 On this basis, the information requirement is not fulfilled.

2.3. Information regarding data sharing

52 The opt-out registrant's registration for the Substance (Registration No. [redacted]) contains a study on surface tension of aqueous solutions (2018) which is adequate for this information requirement. In accordance with Title III of the REACH Regulation, you may request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing).

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

3. Skin sensitisation

54 Skin sensitisation is an information requirement under Annex VII to REACH (Section 8.3.). Under Section 8.3., Column 1, the registrants must submit information allowing (1) A) a conclusion whether the substance is a skin sensitiser and B) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), and (2) risk assessment, where required.

3.1. Information provided

55 You have provided:

i. human maximization test (1982) with the Substance.

56 Furthermore, you have adapted this information requirement by using weight of evidence based on the following experimental data:

ii. human patch test (1984) [with 1-hydroxy-2-phenoxyethane, EC No. 204-589-7; **[1]**

iii. human repeated insult patch test (HRIPT) (2012), with 2-methoxyphenyl)methanol; 2-Methoxybenzyl alcohol, EC No. 210-296-5; **[2]**.

3.2. Assessment of the information provided

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

3.2.1. Assessment whether the Substance causes skin sensitisation

3.2.1.1. Adequacy of the study i. for hazard identification

58 According to the ECHA Guidance[2], "The evaluation of data quality includes assessment of adequacy of the information for hazard/risk assessment and C&L purposes". The ECHA Guidance defines adequacy as "the usefulness of data for hazard/risk assessment purposes".

59 You have provided a study (i.) according to the Human Maximization Test (HMT), and you consider that the Substance is not a skin sensitiser as no reactions were seen in the study.

60 The study i. appears to have been designed to establish safe levels for specific intended uses i.e. use in fragrance, it does not investigate the intrinsic properties of the Substance as required for the purpose of hazard identification. In particular, the dose levels used in

[2] ECHA Guidance R.4

this study (8% in petrolatum) is far lower than the doses expected to be used for hazard identification purposes, as for liquids such as the Substance the induction dose should cause mild dermatitis, as indicated by the protocol for the method by Kligman (1966). Therefore, the study does not allow to make a conclusion whether the Substance causes skin sensitisation.

61 Therefore the study does not provide information on the intrinsic properties of the substance and does not allow to make a conclusion whether the Substance causes skin sensitisation.

3.2.2. Weight of evidence adaptation

62 For studies ii. and iii. the following issues were identified.

63 As explained in Section 0.1., your documentation of the weight of evidence is not in line with the requirements of Annex XI, Section 1.2. Therefore, your adaptation is rejected. In addition, ECHA identified endpoint-specific issue(s) regarding the weight of evidence. These are addressed below.

3.2.2.1. Assessment of relevance of provided information

64 Information that can be used to support a weight of evidence adaptation for the information requirements of Section 8.3 at Annex VII includes similar information to that investigated by the internationally recognised in vitro, in chemico and/or in vivo test methods on skin sensitisation. The key investigations of such test methods address each of the 3 key events of skin sensitisation, either individually or in an integrated approach as follows:

1. investigation of cell proliferation in the draining lymph nodes (local lymph node assay), or
2. investigation of local responses in animals or humans (guinea pig assays or human studies), or
3. investigation of molecular interaction with proteins, inflammatory response in keratinocytes and activation of dendritic cells (in vitro and in chemico assays).

65 All the sources of information ii.-iii. provide relevant information on local effects in humans.

66 However, the studies ii.-iii. have the following deficiencies affecting the reliability of their contribution to the weight of evidence approach.

3.2.2.2. Assessment of reliability of the information from the analogue substances (sources of information ii. and iii.)

67 As explained in Section 0.1.2 of the present decision identifies deficiencies of the grouping and read across approach used in your dossier. These finding apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptations.

68 According to the ECHA Guidance[3], "The evaluation of data quality includes assessment of adequacy of the information for hazard/risk assessment and C&L purposes". The ECHA Guidance defines adequacy as "the usefulness of data for hazard/risk assessment purposes". In the context of a weight of evidence adaptation of standard information requirements, the set of information provided must be adequate for hazard identification.

69 You have provided studies according to Human Patch test (study ii.) and Human Repeat Insult Patch Test (study iii.), and you consider that the substances used in those studies are not skin sensitisers.

[3] ECHA Guidance, Chapter R.4, page 1.

70 For study ii., it is stated that the tested substance is used as a preservative in creams at a concentration of [redacted] and Human Patch Testing was performed to verify the (absence of) skin sensitisation potential for this particular use.

71 The study iii. was designed to assess the safety of the tested substance when used in fragrances. Moreover, the Human Repeat Insult Patch Test is intended to confirm the absence of irritation and sensitisation potential and not to investigate intrinsic properties of the substance.

72 This means that the studies ii. and iii. have been designed to establish safe levels for specific intended uses, rather than investigating the intrinsic properties of the Substance as required for the purpose of hazard identification.

73 Therefore, the studies does not allow to make a conclusion whether the Substance causes skin sensitisation.

3.2.2.3. Conclusion on the weight of evidence

74 All the source of information (ii. and iii.) provide relevant information, as they investigate local effects in humans. Due to the deficiencies described above the relevant sources of information address the information requirement only with high uncertainties due to deficiencies as described in section 3.2.2.2 above. Therefore, even when the information from various sources are assessed together give only low confidence (are of low total weight) compared to the information requirement. Therefore, it is not possible to conclude, based on any source of information alone or considered together, on skin sensitisation.

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

3.2.3. No assessment of potency

76 To be considered compliant and enable a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

77 As the currently available data does not allow to conclude whether the Substance causes skin sensitisation (see sections 3.2.1. and 3.2.2. above), this condition cannot be assessed.

3.2.4. Conclusion

78 On this basis, the information requirement is not fulfilled.

3.3. Specification of the study design

79 To fulfil the information requirement for the Substance, information on molecular interaction with skin proteins and/or inflammatory response in keratinocytes and/or activation of dendritic cells (OECD TG 442C and OECD TG 442D and EU B.71/OECD TG 442E) must be provided. Furthermore an appropriate risk assessment is required if a classification of the Substance as a skin sensitiser (Cat 1A or 1B) is warranted.

80 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing (in vitro/in chemico) data or newly generated (in vitro/in chemico) data, in vivo skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

3.4. Information regarding data sharing

81 The opt-out registrant's registration for the Substance (Registration No. [redacted]) contains two studies (1. OECD Guideline 442C (In Chemico Skin Sensitisation: Direct Peptide Reactivity Assay ([redacted], 2018) and 2. OECD Guideline 442D (In Vitro Skin Sensitisation: ARE-Nrf2 Luciferase Test Method)) which are adequate for this information requirement. In accordance with Title III of the REACH Regulation, you may request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing).

82 In the comments to the draft decision, you indicate that you "will make every effort to reach an agreement on data sharing with opt-out registrant".

4. In vitro gene mutation study in bacteria

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

4.1. Information provided

84 You have adapted this information requirement by using weight of evidence based on the following experimental data:

i. in vitro gene mutation study in bacteria (1992), Methyl benzoate, EC No. 202-259-7; **[3]**, using the following strains: S. typhimurium, other: TA97, TA98, TA100, TA1535, TA1537

ii. in vitro gene mutation study in bacteria (1992), 1-Phenylethanol, EC No. 202-707-1, **[4]**, using the following strains: S. typhimurium TA 1535, TA 1537, TA 98, TA 100 and TA 102.

4.2. Assessment of the information provided

85 As explained in Section 0.1., your documentation of the weight of evidence is not in line with the requirements of Annex XI, Section 1.2. Therefore, your adaptation is rejected. In addition, ECHA identified endpoint-specific issue(s) regarding the weight of evidence. These are addressed below.

4.2.1. Assessment of relevance of provided information

86 For this endpoint your study needs to have key elements foreseen to be investigated in an OECD TG 471 test. The key element investigated by this test is detection and quantification of gene mutations (base pairs, substitution or frame shift) in cultured bacteria including data on the number of revertant colonies.

87 The studies investigate the above mentioned key element. Therefore, they provide information that would contribute to the conclusion on this key element.

4.2.2. Assessment of reliability of the information from the analogue substances

88 However, the reliability of the source of information i. and ii. is significantly affected by the deficiencies identified in section 0.1.1.

89 In addition, the reliability of the source of information i. is also significantly affected by the following issue.

90 The following specifications of OECD TG 471 (2020) applies:

a) The test must be 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)

91 The study i. is described as In vitro gene mutation study in bacteria. However, the following specifications are not according to the requirements of OECD TG 471 (2020):

a) Missing results for the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

4.2.3. Conclusion

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

93 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on this information requirement. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

4.3. Specification of the study design

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

95 In the comments to the draft decision, you have attached a copy of a Robust Study Summary (RSS). The RSS includes the information listed above as missing in the dossier. You have proposed to update your dossier with the modified RSS.

96 The information provided as part of your comments addresses the incompliances 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.

5. Short-term toxicity testing on aquatic invertebrates

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

5.1. Information provided

98 You have adapted this information requirement by using a weight of evidence approach in accordance with Annex XI, Section 1.2. You have provided the following sources of information:

i. EU Method C.2 study with the analogue substance **[11]**;
ii. OECD TG 202 study with the analogue substance **[10]**.

5.2. Assessment of the information provided

99 We have assessed this information and identified the following issues:

100 As explained in Section 0.1.2., your documentation of the weight of evidence is not in line with the requirements of Annex XI, Section 1.2. Therefore, your adaptation is rejected. In addition, ECHA identified endpoint-specific issue(s) regarding the weight of evidence. These are addressed below.

5.2.1. Assessment of relevance of provided information

101 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.1. at Annex VII includes similar information that is produced by the OECD TG 202. OECD TG 202 requires the study to analyse the following key investigation: the concentration of the test material leading to the immobilisation of 50% of daphnids (EC50) at the end of the test is estimated.

102 The sources of information (i. and ii.) provide relevant information on key investigation, i.e. both sources provide EC50 after 48 hours of exposure to the test material, but, as explained below, have the following deficiencies affecting their reliability.

5.2.2. Assessment of reliability of the information from the analogue substances

103 For the experimental study relevant for this information requirement, i.e. OECD TG 202, the following technical specifications must be met:

- the test design is reported (*e.g.* static or semi-static test, number of replicates);
- the test procedure is reported (*e.g.* composition of the test medium, loading in number of *Daphnia* per test vessel);
- 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;
- the dissolved oxygen and pH measured at least at the beginning and end of the test is reported;
- adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided.

104 The information listed above is not reported in the registration dossier for neither of the sources of information (i. and ii.). Therefore, the reporting of the studies is not sufficient to conduct an independent assessment of its reliability.

105 Thus, as explained in section 0.1.1. above the information from the analogue substances submitted under your weight of evidence adaptation is not considered reliable.

5.2.3. Conclusion

106 Your sources of information provide information on key investigation but, in the absence of reliable information, no conclusion can be drawn on key investigation as required by the information requirement.

107 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on this information requirement. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

5.3. Information regarding data sharing

108 The opt-out registrant's registration for the Substance (Registration No. [redacted]) contains a Daphnia sp., Acute Immobilisation Test (2018) which is adequate for this information requirement. In accordance with Title III of the REACH Regulation, you may request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing).

109 In the comments to the draft decision, you indicate that you "will make every effort to reach an agreement on data sharing with opt-out registrant". Furthermore, you note that you

"will consider this request and will perform the testing according to internationally accepted standard test guideline, in case there is a failure of agreement on data sharing".

6. Growth inhibition study aquatic plants

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

6.1. Information provided

111 You have adapted this information requirement by using a weight of evidence approach in accordance with Annex XI, Section 1.2. You have provided the following sources of information:

i. Scenedesmus cell proliferation inhibition test, DIN 38412 part 9 with the analogue substance **[11]**;

ii. Experimental study ("*The objective of the study was to determine effective concentration of test chemical on aquatic algae.*") with the analogue substance **[12]**.

6.2. Assessment of the information provided

112 We have assessed this information and identified the following issues:

113 As explained in Section 0.1.2., your documentation of the weight of evidence is not in line with the requirements of Annex XI, Section 1.2. Therefore, your adaptation is rejected. In addition, ECHA identified endpoint-specific issue(s) regarding the weight of evidence. These are addressed below.

6.2.1. Assessment of relevance of provided information

114 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.1. at Annex VII includes similar information that is produced by the OECD TG 201. OECD TG 201 requires the study to analyse the following key investigations: the concentrations of the test material leading to a 50 % (EC50) and 0% (or 10%) (EC0 and EC10) inhibition of growth at the end of the test are estimated.

115 The source of information i. provides relevant information on key investigations, i.e. EC50 and EC10 after 72 hours of exposure to the test material. The source of information ii. provides partially relevant information on key investigations, i.e. EC50 after 96 hours of exposure to the test material. However, both sources of information have the following deficiencies affecting their reliability.

6.2.2. Assessment of reliability of the information from the analogue substances

116 For the experimental study relevant for this information requirement, i.e. OECD TG 201, the following technical specifications must be met:

- the test design is reported (*e.g.*, number of replicates, number of test concentrations and geometric progression used);
- the test conditions are reported (*e.g.*, composition of the test medium, test temperature, test species, biomass density at the beginning of the test);
- the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported;

- the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;
- microscopic observation performed to verify a normal and healthy appearance of the inoculum culture are reported. Any abnormal appearance of the algae at the end of the test is reported;
- adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided.

117 The information listed above is not reported in the registration dossier for neither of the sources of information (i. and ii.). Therefore, the reporting of the studies is not sufficient to conduct an independent assessment of its reliability.

118 Thus, as explained in section 0.1.1. above the information from the analogue substances submitted under your weight of evidence adaptation is not considered reliable.

6.2.3. Conclusion

119 Your sources of information provide information on key investigation but, in the absence of reliable information, no conclusion can be drawn on key investigation as required by the information requirement.

120 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on this information requirement. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

6.3. Information regarding data sharing

121 The opt-out registrant's registration for the Substance (Registration No. [redacted]) contains a Freshwater Alga and Cyanobacteria, Growth Inhibition Test (2018) which is adequate for this information requirement. In accordance with Title III of the REACH Regulation, you may request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing).

122 In the comments to the draft decision, you indicate that you "will make every effort to reach an agreement on data sharing with opt-out registrant". Furthermore, you note that you "will consider this request and will perform the testing according to internationally accepted standard test guideline, in case there is a failure of agreement on data sharing".

Reasons related to the information under Annex VIII of REACH

7. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

123 An in vitro cytogenicity study in mammalian cells or an in vitro micro-nucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

7.1. Information provided

124 You have adapted this information requirement by using weight of evidence based on the following experimental data:

i. in vitro mammalian chromosome aberration test, according to OECD TG473 (1999), with Ethylbenzene EC No. 202-849-4 **[5]**;

ii. in vitro mammalian chromosome aberration test, according to OECD TG473 (2018), with 2-Methoxynaphthalene EC No.202-213-6 **[6]**.

7.2. Assessment of the information provided

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

126 As explained in Section 0.1., your documentation of the weight of evidence is not in line with the requirements of Annex XI, Section 1.2. Therefore, your adaptation is rejected. In addition, ECHA identified endpoint-specific issue(s) regarding the weight of evidence. These are addressed below.

7.2.1. Assessment of relevance of provided information

127 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.2. at Annex VIII includes:

- Detection and quantification of cytotoxicity and the frequency of cells with structural chromosomal aberration(s) or the frequency of micronuclei in cultured mammalian cells *(in vitro*) or in mammals (*in vivo*).

128 A level of information on these aspects similar to that obtained from in vitro/in vivo chromosomal aberration tests (OECD TG 473/OECD TG 475) or in vitro/in vivo micronucleus tests (OECD TG 487/OECD TG 474) is required. The sources of information provide relevant information on detection and quantification of gene mutation in cultured mammalian cells. However, these sources of information have the following deficiencies affecting their reliability.

7.2.2. Assessment of reliability of the information from the analogue substances

129 The reliability of sources of information i. and ii. is significantly affected by the deficiencies identified in the section 0.1.1.

130 In addition, source of information i. has the following deficiencies:

131 Testing in accordance with OECD TG 473 requires that the following specifications/ conditions have to be met:

a) The maximum concentration tested must induce 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration must correspond to 10 mM, 2 mg/mL or 2 µl/mL, whichever is the lowest.
b) At least 300 well-spread metaphases must be scored per concentration.

c) Data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures must be reported.

132 The study i. is described as in vitro mammalian chromosome aberration test. However, the study is not according to the requirements of OECD TG 473 because:

a) the maximum tested concentration is not 10 mM, 2 mg/mL or 2 µl/mL, or that induced 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance;
b) the scoring is of less than 300 metaphases per concentration;
c) no data on the cytotoxicity and/or the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures is reported.

133 Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the conditions as specified in the corresponding OECD TG.

134 In the absence of such information on those critical aspects of the specification/conditions of the provided studies, ECHA cannot evaluate the reliability of the conclusions on cytotoxicity and the frequency of cells with structural chromosomal aberration(s).

135 In summary, the sources of information (i) and (ii) have significant reliability issues and cannot contribute to the conclusion on the potential of the Substance to cause cytotoxicity and cannot provide information on the frequency of cells with structural chromosomal aberration(s) or the frequency of micronuclei in cultured mammalian cells.

7.2.3. Conclusion

136 It is not possible to conclude, based on any source of information alone or considered together, on this information requirement. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

7.3. Specification of the study design

137 To fulfil the information requirement for the Substance, either in vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or in vitro micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

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

8. In vitro gene mutation study in mammalian cells

138 An in vitro gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the in vitro gene mutation test in bacteria and the in vitro cytogenicity .

139 Your dossier contains an adaptation for an in vitro gene mutation study in bacteria, and an adaptation for an in vitro cytogenicity study in mammalian cells or in vitro micronucleus study.

140 The information for the in vitro gene mutation study in bacteria and for the in vitro cytogenicity study in mammalian cells or in vitro micronucleus study provided in the dossier are rejected for the reasons provided in sections 0.1, 4 and 7.

141 The result of the requests for an in vitro gene mutation study in bacteria and for an in vitro cytogenicity study in mammalian cells will determine whether the present requirement for

an in vitro mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

142 Consequently, you are required to provide information for this endpoint, if the in vitro gene mutation study in bacteria, the in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study provides a negative result.

8.1. Information provided

143 You have adapted this information requirement by using weight of evidence based on the following experimental data:

i. in vitro mammalian cell gene mutation test (2015) with 1-phenylethanol EC No. 202-707-1, [**4**].

ii. in vitro mammalian cell gene mutation test (2015) with 2-phenylethyl phenylacetate EC no. 203-013-1, [**7**]

8.2. Assessment of the information provided

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

145 As explained in Section 0.1., your documentation of the weight of evidence is not in line with the requirements of Annex XI, Section 1.2. Therefore, your adaptation is rejected. In addition, ECHA identified endpoint-specific issue(s) regarding the weight of evidence. These are addressed below.

8.2.1. Assessment of relevance of provided information

146 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.3 at Annex VIII includes similar information that is produced by the OECD TG 476/490 and OECD TG 488. This includes:

a) Detection and quantification of gene mutations (point mutations, frame-shift mutations, small deletions, etc.) including data on the frequency of mutant colonies in cultured mammalian cells (*in vitro*) or mutant frequency for each tissue in mammals (*in vivo*).

147 The sources of information i. and ii. provide relevant information on detection and quantification of gene mutation in cultured mammalian cells.

8.2.2. Assessment of reliability of the information from the analogue substances

148 However, these sources of information have deficiencies affecting their reliability as identified and explained in section 0.1.1.

8.2.3. Conclusion

149 In summary, even though the sources of information i. and ii. provide relevant information, they have a significant reliability issue and cannot contribute to the conclusion on the potential of the Substance to cause gene mutations.

150 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on this information requirement. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

8.3. Specification of the study design

151 To fulfil the information requirement for the Substance, either the in vitro mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

8.4. Information regarding data sharing

152 The opt-out registrant's registration for the Substance (Registration No. [redacted]) contains an In Vitro Mammalian Cell Gene Mutation Test (2018) which is adequate for this information requirement. In accordance with Title III of the REACH Regulation, you may request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing).

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

9. Short-term repeated dose toxicity (28 days)

154 A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII to REACH (Section 8.6.1.).

9.1. Information provided

155 You have provided:

i. short-term repeated dose toxicity (2019) with the Substance.

9.2. Assessment of the information provided

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

157 To fulfil the information requirement, the short-term toxicity study (28 days) must meet the requirements of OECD TG 407. Therefore, the following specifications must be:

a. highest dose level should aim to induce toxicity or reach the limit dose.

158 The study i. is described as short-term repeated dose toxicity according to OECD TG 407. However, the following specifications are not according to the requirements of OECD TG 407:

a. no justification for the dose setting while the highest dose levels tested was 450 mg/kg bw/d, which is below the limit dose of the test guideline, and no adverse effect were observed.

9.2.1. Conclusion

159 Based on the above, the information you provided do not fulfil the information requirement.

9.3. Specification of the study design

160 Following the criteria provided in Annex VIII, Section 8.6.1, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance; Guidance on IRs and CSA, Section R.7.5.6.3.1.

161 When there is no information available neither for the 28-day repeated dose toxicity endpoint (EU B.7, OECD TG 407), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers

the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1. (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

162 For information on the study design see request for OECD TG 422 below.

10. Screening for reproductive/developmental toxicity

163 A screening for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII to REACH (Section 8.7.1.), if there is no evidence from analogue substances, QSAR or in vitro methods that the substance may be a developmental toxicant.

10.1. Information provided

164 You have adapted this information requirement by using weight of evidence based on the following experimental data:

i. Combined Repeated and Reproduction/ Developmental Toxicity Screening Test (2016) with Methyl phenyl acetate EC no. 202-940-9 **[13]**

ii. Repeated dose 28-day Oral Toxicity study,(2014) with Benzyl propionate EC no. 204-559-3 **[8]**.

10.2. Assessment of the information provided

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

166 As explained in Section 0.1., your documentation of the weight of evidence is not in line with the requirements of Annex XI, Section 1.2. Therefore, your adaptation is rejected. In addition, ECHA identified endpoint-specific issue(s) regarding the weight of evidence. These are addressed below.

10.2.1. Assessment of relevance of provided information

167 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.

168 1) Sexual function and fertility

169 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.

170 The study i. provides relevant information on sexual function and fertility. However, the study ii. provides only limited information on sexual function and fertility. More specifically, 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.

171 However, these sources of information have deficiencies affecting their reliability as identified and explained in section 0.1.2. within Reasons common to several requests.

172 2) Toxicity to offspring

173 Information on pre- and perinatal developmental toxicity reflected by litter sizes, post-implantation 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.

174 The study i. provides relevant information on toxicity to offspring, however, the study ii. does not provide information on toxicity to offspring.

175 The reliability of study i., however, is significantly affected for the reason provided above under 1).

176 3) Systemic toxicity

177 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.

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

179 The reliability of these studies, however, is significantly affected for the reason provided above under 1).

10.2.2. Conclusion

180 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.

181 Therefore, it is not possible to conclude based on any source of information alone or considered together, on this information requirement. Thus, your adaptation is rejected and the information requirement is not fulfilled.

182 On this basis, the information requirement is not fulfilled.

10.3. Specification of the study design

183 A study according to the test method EU B.64/OECD TG 422 must be performed in rats.

184 The study must be conducted with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

10.4. Information regarding data sharing obligations

185 The opt-out registrant's registration for the Substance (Registration No. [redacted]) contains a combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test (2018) which is adequate for this information requirement. In accordance with Title III of the REACH Regulation, you must request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing).

186 In the comments to the draft decision, you indicate that you "will make every effort to reach an agreement on data sharing with opt-out registrant".

11. Short-term toxicity testing on fish

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

11.1. Information provided

188 You have adapted this information requirement by using (a) weight of evidence approach in accordance with Annex XI, Section 1.2. You have provided the following sources of information:

i. Experimental study "*Determination of the effect of water constituents Fish, DIN 38 412*" with the analogue substance **[9]**

ii. Experimental study where "*Tidewater silversides (Menidia beryllina) were exposed to a range of concentrations of test chemical for a period of 96 hr using static method.*" with the analogue substance **[10]**

iii. OECD TG 203 study with the Substance.

11.2. Assessment of the information provided

189 We have assessed this information and identified the following issues:

190 As explained in Section 0.1.2., your documentation of the weight of evidence is not in line with the requirements of Annex XI, Section 1.2. Therefore, your adaptation is rejected. In addition, ECHA identified endpoint-specific issue(s) regarding the weight of evidence. These are addressed below.

11.2.1. Assessment of relevance of provided information

191 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.1.1. at Annex VII includes similar information that is produced by the OECD TG 203. OECD TG 203 requires the study to analyse the following key investigation: the concentration of the test material leading to the mortality of 50% of the juvenile fish (LC 50) at the end of the test is estimated.

192 All the sources of information (i., ii. and iii.) provide relevant information on key investigation, i.e. all sources provide LC50 after 96 hours of exposure to the test material, but, as explained below, have the following deficiencies affecting their reliability.

11.2.2. Assessment of reliability of the information provided

193 For the experimental study relevant for this information requirement, i.e. OECD TG 202, the following technical specifications must be met:

- the analytical measurement of test concentrations is conducted (validity criterion);
- the test procedure is reported (*e.g.* composition of the test medium, fish loading);
- adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations are provided;
- mortalities and sub-lethal effects (*e.g.* with regard to equilibrium, appearance, ventilator and swimming behaviour) are reported. The frequency of observations includes at least 2 observations within the first 24 hours and at least two

observations per day from day 2 to 4;

194 Your registration dossier provides the following information:

- that no analytical measurement of test concentrations was conducted for the information sources i. and iii.;
- on the test procedure, you have not specified composition of the test medium and fish loading for the information sources i. and ii.;
- for the source of information ii.: on the analytical method, adequate information, i.e. the method used, performance parameters of the method, is not reported. The results of the analytically determined exposure concentrations are not provided;
- tabulated data on mortalities and sub-lethal effects (e.g. with regard to equilibrium, appearance, ventilator and swimming behaviour) obtained on at least 2 observations within the first 24 hours and at least two observations per day from day 2 to 4 for each treatment group and control are not reported for the information sources i. and ii.

195 Based on the above, there is no information on analytical verification of exposure concentrations in any of the reported studies. Therefore, you have not demonstrated that effect values can reliably be based on nominal test material concentrations. Furthermore, the reporting of the studies for the sources of information i. and ii. is not sufficient to conduct an independent assessment of its reliability.

196 Consequently, no reliable predictions can be made from the studies with the analogue substances (sources of information i. and ii.) as well as source of information iii. cannot reliably inform on the key investigation.

197 For these reasons and those explained in section 0.1.1, the information from the analogue substances and from the Substance submitted under your weight of evidence adaptation is not considered reliable.

11.2.3. Conclusion

198 Your sources of information provide information on key investigation but, in the absence of reliable information, no conclusion can be drawn on key investigation as required by the information requirement.

199 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on this information requirement. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

11.3. Information regarding data sharing obligations

200 The opt-out registrant's registration for the Substance (Registration No. [redacted]) contains a fish, acute toxicity test (2018) which is adequate for this information requirement. In accordance with Title III of the REACH Regulation, you must request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing).

201 In the comments to the draft decision, you indicate that you "will make every effort to reach an agreement on data sharing with opt-out registrant".

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).

All Guidance on REACH is 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 8 July 2021.

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).

One addressee was removed from Appendix 3 as that registrant has opted out from all information requirements addressed in this decision.

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.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

Appendix 3: Addressees 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]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

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[4].

(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 shall 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 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[5].

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