~~Confidential~~

Helsinki, 17 January 2023

Addressees
Registrant(s) of bis 2EH maleate JS [205-524-5] as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
20/04/2020

Registered substance subject to this decision ("the Substance")
Substance name: Bis(2-ethylhexyl) maleate
EC number: 205-524-5

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 ***22 October 2025***.

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) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102

2. Long-term toxicity testing on aquatic invertebrates also requested below (triggered by Annex VII, Section 9.1.1., column 2)

3. 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

4. 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)

5. Long-term toxicity testing on fish also requested below (triggered by Annex VIII, Section 9.1.3., column 2)

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

6. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats

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

8. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210)

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.

In the requests above, the same study has been requested under different Annexes. This is because some information requirements may be triggered at lower tonnage band(s). In such cases, only the reasons why the information requirement is triggered are provided for the lower tonnage band(s). For the highest tonnage band, the reasons why the standard information requirement is not met and the specification of the study design are provided. Only one study is to be conducted; all registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the others under Article 53 of REACH.

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) adaptation in accordance with Annex XI, section 1.2:

Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)

2 In your comments to the draft decision you state that "the approach applied should be called a "Weight of evidence inside a read across", not the other way around." ECHA notes that this is not clear from the dossier which still suggests a general weight of evidence approach. Therefore, this section is kept in this decision. The read-across elements, however, are fully assessed under Section 1.5 of Annex XI, taking your arguments of weight of evidence embedded into it into account.

3 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.

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

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

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

7 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. The common deficiencies are set out here, while the specific ones are set out under the information requirement concerned in the Appendices below.

8 These issues identified below are essential for all the information requirements in which you invoked a weight of evidence.

0.1.1. Reliability of the read across approach

9 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.

10 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.

11 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).

0.1.2. Predictions for toxicological properties

12 You provide a read-across justification document in IUCLID Section 13.

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

- Source substance 1, dibutyl maleate, EC No. 203-328-4.
- Source substance 2, furan-2,5-dione (or maleic anhydride), EC No. 203-571-6.

14 You provide the following reasoning for the prediction of toxicological properties of the Substance (DOM) for reproductive toxicity and developmental toxicity:

15 "Based on the metabolism of diesters and structural related substances similarities, dibutyl maleate (DBM), maleic anhydride / maleic acid, and 2-ethylhexan-1-ol were selected as the most suitable read-across substances for DOM, as they represent metabolic/chemical breakdown products of DOM.

16 Maleic acid results from the complete de-esterification and/or chemical hydrolysis of DOM. Although hydrolysis of DOM (either enzymatic or non-enzymatic) most likely results in the formation of maleic acid as a metabolite, maleic anhydride was included as a potential read-across candidate because of its high reactivity with water, which means that it is rapidly converted to maleic acid in biological systems."

17 For sub-chronic toxicity (90-day) there was no read-across justification available. As explained above, ECHA understands that your read-across hypothesis applies for sub-chronic toxicity (90-day). ECHA understands also that your read-across hypothesis is based on the formation of common (bio)transformation products. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

18 We have identified the following issue(s) with the prediction(s) of toxicological properties:

0.1.2.1. Read-across hypothesis contradicted by existing data

19 Annex XI, Section 1.5. provides that "substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances". The Guidance on IRs and CSA, Section R.6.2.2.1.f. indicates that "it is important to provide supporting information to strengthen the rationale for the read-across". 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 substances.

20 The observation of differences in the toxicological properties between the source substance(s) and the Substance would contradict the hypothesis that the properties of the Substance can be predicted from the data on the source substances. An explanation why such differences do not affect the read-across hypothesis must be provided and supported by scientific evidence.

21 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar Substance and source substances cause the same type of effect(s).

22 The pituitary and thyroid histopathology findings were reported exclusively for the Substance (combined repeated dose toxicity study with the reproduction/developmental toxicity screening test 2010).

23 In your comments to the draft decision you state that "bilateral thyroid follicular cell hypertrophy following changes in thyroid hormone levels and concurrent hypertrophy of thyroid-stimulating hormone–producing cells (thyrotrophs) in the pituitary pars distalis (predominantly seen in male rats) is known from the published literature (Zabka et al. 2011)." You conclude in your comments that "the findings in the current study were regarded non-adverse based on the following conditions (Kerlin et al., 2016, Lewis et al., 2002):

- *The change represented an adaptive response (liver enlargement and hepatocellular hypertrophy due to enzyme induction)*
- *The severity was limited (microscopic findings were all recorded only at minimal degree)*
- *the findings in thyroid gland and pituitary gland were regarded secondary to the non-adverse liver findings*".

24 ECHA acknowledges your comment and concludes that you have not demonstrated the secondary nature or the adversity of the thyroid histopathological findings. This is because thyroid hormone levels were not measured in the available repeated dose toxicity studies, and the historical control data supporting the claimed normal background pathology are not included in your documentation.

25 Regardless of the (non)adversity of the histopathological findings, the available set of data on the Substance and on the source substances indicates differences in the toxicological properties of the substances. This contradicts your read-across hypothesis whereby the Substance and source substances cause the same type of effect(s). Therefore you have not demonstrated and justified that the properties of the source substance(s) and of the Substance are likely to be similar despite the observation of these differences.

26 Additional issues with your weight of evidence adaptation are addressed under the section corresponding to the information requirement.

0.2. Triggering of long-term toxicity testing on aquatic invertebrates and fish

27 This section applies to long-term toxicity testing on aquatic invertebrates under Annex VII and on fish under Annexes VIII.

28 Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests does not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (Guidance on IRs and CSA, Section R.7.8.5).

29 In the provided OECD TG 105 (2010), the saturation concentration of the Substance in water was determined to be < 36 µg/L.

30 Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates and fish must be provided.

Reasons related to the information under Annex VII of REACH

1. In vitro gene mutation study in bacteria

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

1.1. Information provided

32 You have provided:

i. *In vitro* gene mutation study in bacteria (1999) with the Substance.

ii. *In vitro* gene mutation study in bacteria (1990) with the Substance.

1.2. Assessment of the information provided

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

1.2.1. Studies not adequate for the information requirement

34 To fulfil the information requirement, the study must meet the requirements of OECD TG 471 (2020), which includes:

- 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)

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

- results for the appropriate 5 strains, that includes the required fifth strain, S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101).

36 The information provided does not cover one of the key parameters required by OECD TG 471.

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

1.3. Specification of the study design

38 To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471, 2020) must be performed using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.

39 In your comments to the draft decision you agree with the request.

2. Long-term toxicity testing on aquatic invertebrates

40 Short-term toxicity testing on aquatic invertebrates is an information requirement under Column 1 of Annex VII to REACH (Section 9.1.1.). However, long-term toxicity testing on aquatic invertebrates must be considered (Section 9.1.1., Column 2) if the substance is poorly water soluble.

41 As explained under section 0.2 above the Substance is poorly soluble and information on long-term toxicity on aquatic invertebrates must be provided.

42 You have provided 3 short-term toxicity studies on aquatic invertebrates, but no information on long-term toxicity on aquatic invertebrates for the Substance.

43 The examination of the information provided, as well as the selection of the requested test and the test design are addressed under section 8 below.

3. Growth inhibition study aquatic plants

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

3.1. Information provided

45 You have provided a study according to OECD TG 201 with the Substance.

3.2. Assessment of the information provided

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

47 To fulfil the information requirement, a study must comply with OECD TG 201 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the concentrations of the test material are measured at least at the beginning and end of the test:

   i. at the highest, and

   ii. at the lowest test concentration, and

   iii. at a concentration around the expected EC_{50}.

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

c) adequate information on the results of the analytical determination of exposure concentrations is provided.

48 Your registration dossier provides an OECD TG 201 study showing the following:

- tabulated data on the algal biomass determined daily for each treatment group and control are not reported; the results of the analytical monitoring of exposure concentrations for each test concentration is not reported.

- In the comments to the draft decision you have provided tabulated data on the algal biomass and on the results of the determination of exposure.

49 The tabulated data in the comments on the draft decision indicates that the validity criteria of OECD TG 201 are met.

50 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.

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

3.3. Study design and test specifications

52 The Substance is difficult to test due to the low water solubility (< 36 µg/l, OECD TG 105) and adsorptive properties (log Kow of 7.24, OECD TG 117). OECD TG 201 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 201. 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.

Reasons related to the information under Annex VIII of REACH

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

53 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.).

4.1. Information provided

54 You have provided:

i. *In vitro* chromosome aberration study in mammalian cells (1998) with the Substance.

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

4.1.1. Study not adequate for the information requirement

56 To fulfil the information requirement the study has to be an in vitro chromosomal aberration test or an in vitro micronucleus test, conducted in mammalian cells in accordance with OECD TG 473 or OECD TG 487, respectively (Guidance on IRs and CSA, Table R.7.7–2). Therefore, the following specifications must be:

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) The response for the concurrent negative control must be inside the historical control range of the laboratory.
c) Data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures must be reported.

57 The study i. is described as in vitro chromosome aberration study in mammalian cells. However, the following specifications are not according to the requirements of OECD TG 473:

a) a maximum tested concentration of 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) a negative control with a response inside the historical control range of the laboratory.
c) data on the cytotoxicity and/or the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures.

58 More specifically, the robust study summary provided in the dossier did not inform on the above specifications of the study i.

59 In the comments to the draft decision you provided the missing specifications supporting study i. 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.

60 The information provided in the dossier does not cover key parameters required by OECD TG 473.

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

4.2. Specification of the study design

62 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.

5. Long-term toxicity testing on fish

63 Short-term toxicity testing on fish is an information requirement under Column 1 of Annex VIII to REACH (Section 9.1.3.). However, long-term toxicity testing on fish must be considered (Section 9.1.3., Column 2) if the substance is poorly water soluble.

64 As already explained under section 0.2 above, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

65 You have provided 3 short-term toxicity studies on fish, but no compliant information on long-term toxicity on fish for the Substance.

66 The examination of the information provided, as well as the selection of the requested test and the test design are addressed under section section 9 below.

Reasons related to the information under Annex IX of REACH

6. Sub-chronic toxicity study (90-day)

67 A sub-chronic toxicity study (90 day) is an information requirement under Annex IX to REACH (Section 8.6.2.).

6.1. Information provided

68 You have adapted this information requirement by using weight of evidence and read-across based on the following experimental data:

i. Justification: "*In the absence of significant data with dioctyl maleate itself, a weight of evidence approach was applied. Because of the chemical similarities of dioctyl maleate to n-butyl maleate and dibutyl maleate, the available repeated-dose toxicity data should be sufficient for read-across assessment. Animal studies showed that the main target organs were the kidneys*."

ii. Sub-chronic toxicity study (2010) with source substance 1 via oral route.

iii. Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (2010) with the Substance via oral route.

iv. Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (1993) with source substance 1 via oral route.

v. 6-Month repeated dose toxicity study in rats, hamsters and monkeys (1988) with source substance 4 via inhalation route.

6.2. Assessment of the information provided

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

6.2.1. Rejected weight of evidence

70 ECHA identified endpoint-specific issue(s) regarding the weight of evidence. These are addressed below.

6.2.1.1. Studies not relevant or reliable for the information requirement

71 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.6.2 at Annex IX includes, at general level, information on systemic toxicity in intact, non-pregnant and young adult males and females from: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity. Information should address effects on the following physiological systems: circulatory system, digestive/excretory system, endocrine system, immune system, integumentary system, musculoskeletal system, nervous system, renal/urinary system, reproductive system, and respiratory system.

72 The studies ii. to iv. investigate the above key parameters.

73 The study v. has been conducted using no recognised testing guideline and has a limited reporting of the study. It does not provide information on blood chemistry nor full histopathology. Therefore, this source of information is only partially relevant. Even though study v. does partly cover the above key parameters, there are significant reliability issues

with your documentation of the read-across approach that are not in line with the requirements of Annex XI, Section 1.5, as explained in Section 0.1.

74 In your comments to the draft decision you conclude that "ECHA does not object to the read across approach" related to study ii. ECHA disagrees with your conclusion because, even though study ii. does cover the above key parameters, there are significant reliability issues with your documentation of the read-across approach that are not in line with the requirements of Annex XI, Section 1.5, as explained in Section 0.1. Because of the issues related to the requirements of Annex XI, Section 1.5 alone, study ii., or studies iv. and v., cannot fulfil the information requirement.

6.2.1.1.1. Repeated dose toxicity: oral

75 OECD TG 408 includes the following specifications:

i. exposure duration of 90 days.

76 The studies iii. and iv. are sub-acute toxicity studies.

77 Study iii. has an exposure duration of 42 days. Study iv. has exposure duration of at least 46 days for males and females.

78 The studies iii. and iv. do not cover this specification of the OECD TG 408.

79 Further, the study iv. has the same significant reliability issues as already mentioned in section 0.1.

6.3. Specification of the study design

80 Following the criteria provided in Annex IX, Section 8.6.2, 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.7.5.6.3.2.

81 According to the OECD TG 408, the rat is the preferred species.

7. Long-term toxicity testing on aquatic invertebrates

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

7.1. Information provided

83 You have provided a study "according to OECD 202, part II which is nowadays published as OECD 211".

7.2. Assessment of the information provided

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

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

86 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.

87 Your registration dossier provides a study "according to OECD 202, part II which is nowadays published as OECD 211" showing the following:

a) no analytical monitoring of exposure was conducted.

88 Based on the above, there is critical methodological deficiency resulting in the rejection of the study results. Therefore, the requirements of OECD TG 211 are not met.

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

90 In your comments to the draft decision you agree with the request.

7.3. Study design and test specifications

91 OECD TG 211 specifies 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' under Section 3.3 above.

8. Long-term toxicity testing on fish

92 Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

8.1. Information provided

93 You have provided the following information:a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification: "A long-term toxicity study to fish does not need to be conducted as the outcome of the chemical safety assessment does not indicate a need for further investigation."

8.2. Assessment of the information provided

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

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

96 Your adaptation is therefore rejected.

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

98 In your comments to the draft decision you agree with the request.

8.3. Study design and test specifications

99 To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (Guidance on IRs and CSA, Section R.7.8.2.).

100 OECD TG 210 specifies 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' under Section 3.3 above.

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 4 May 2021.

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

Based on the clarification provided in your comments to the draft decision, ECHA has removed the following request from this decision: Pre-natal developmental toxicity (Annex IX, Section 8.7.2).

ECHA took into account your comments and amended the request(s) and the deadline.

In your comments on the draft decision, you requested an extension of the deadline to provide information from 18 to 30 months from the date of adoption of the decision. You justified your request with a statement from a testing laboratory. The deadline of the decision was 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.

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: 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]
[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[2].

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.
- 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[3].

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