~~Confidential~~

Helsinki, 24 May 2024

Addressees
Registrants of JS_103242_FEUC as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
26 March 2013

Registered substance subject to this decision ("the Substance")
Substance name: Bis(2-ethylhexyl) azelate
EC/List number: 203-091-7

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 ***30 August 2027***.

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

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

1. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

2. 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

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

4. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

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

The reasons for the request(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 or for different information requirements.

In the case of the same study 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.

In all cases, 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 request(s)
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

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

Appendix 1: Reasons for the request(s)

Reasons common to several requests

0.1. Read-across adaptation rejected

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

- *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.)
- Pre-natal developmental toxicity study, one species (Annex IX, Section 8.7.2.)

2 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.

3 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.

4 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).

0.1.1. Scope of the grouping of substances (category)

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

6 For the purpose of this decision, the following abbreviations are used for the source substance(s)/category members:

i. CAS 6938-94-9 / EC 230-072-0 / Diisopropyl adipate

ii. CAS 105-99-7 / EC 203-350-4 / Dibutyl adipate

iii. CAS 110-33-8 / EC 203-757-7 / Dihexyl adipate

iv. CAS 1330-86-5 / EC 215-553-5 / Diisooctyl adipate

v. CAS 123-79-5 / EC 204-652-9 / Dioctyl adipate

vi. CAS 103-23-1 / EC 203-090-1 / Bis(2-ethylhexyl) adipate (DEHA)

vii. CAS 68515-75-3 / EC 271-105-9 / Hexanedioic acid, di-C7-9-branched and linear alkyl esters

viii. CAS 33703-08-1 / EC 251-646-7 / Diisononyl adipate

ix. CAS 16958-92-2 / EC 241-029-0 / Bis(tridecyl) adipate

x. CAS 85117-94-8 / EC 285-645-8 / Bis(2-octyldodecyl) adipate

xi. CAS 103-24-2/ EC 203-091-7 / Bis(2-ethylhexyl) azelate (your Substance)

xii. CAS 897626-46-9 / EC 618-295-5 / Bis(2-octyldodecyl) azelate

xiii. CAS 7491-02-3 / EC 231-306-4 / Diisopropyl sebacate

xiv. CAS 109-43-3/ EC 203-672-5 / Dibutyl sebacate

xv. CAS 122-62-3 / EC 204-558-8 / Bis(2-ethylhexyl) sebacate

xvi. CAS 69275-01-0 / EC not available / Bis(2-octyldodecyl) sebacate

7 You justify the grouping of the substances as:

8 "*Due to the structural similarities and consistent trend in physico-chemical, toxicological, ecotoxicological properties and toxicokinetic behaviour, the members of the PFAE linear group can be considered as a category of substances*,…"

9 You define the applicability domain as:

10 "*all members of the category PFAE linear are diester derivatives of the common saturated diacids: namely adipic (C6), azelaic (C9) and sebacic (C10) acid. The alcohol portion of the diesters generally falls in the C3-C20 carbon number range, including linear and branched alcohols*."

11 ECHA understands that this is the applicability domain of the grouping and your predictions are assessed on this basis.

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: category member substance vi.

14 You provide the following reasoning for the prediction of toxicological properties:

15 "*Due to the structural similarities and consistent trend in physico-chemical, toxicological, ecotoxicological properties and toxicokinetic behaviour, the members of the PFAE linear group can be considered as a category of substances*,…"

16 You state the following prediction for the hazardous properties of the category members (including the Substance):

17 "*considering all available evidence and expert judgement the category members showed no acute oral, dermal or inhalation toxicity, no skin irritation, eye irritation or sensitizing properties, no human hazard for systemic toxicity after repeated oral, inhalative and dermal exposure and are not mutagenic or clastogenic and have shown no relevant reproduction toxicity and have no effect on intrauterine development*."

18 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.

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

0.1.2.1. Read-across hypothesis contradicted by existing data

20 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 must strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance(s) (Guidance on IRs and CSA R.6., Section R.6.2.2.1.f.).

21 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 to be provided and supported by scientific evidence.

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

23 You predict no hazardous effects for the category substances but the study results related to skin sensitisation, repeated dose toxicity, mutagenicity, and reproductive/ developmental toxicity obtained with the Substance and the source substance vary and/or contradict your prediction for no hazardous effects.

0.1.2.1.1. Skin sensitisation

24 Positive results for skin sensitisation are observed in the local lymphnode assay (OECD TG 429) conducted with the Substance (xi). These meet the criteria for classification, whereas you have not classified on this basis.

0.1.2.1.2. Repeated dose toxicity

25 Test item related target organ toxicity effects are reported in

- a repeated dose 28-day oral toxicity study (OECD TG 407) conducted with the source substance vi. (increased renal and hepatic weight, hyaline and eosinophilic droplets in kidneys)
- a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) with the Substance xi (clinical chemistry, haematology).

26 No test item related target organ toxicity effects are reported for the repeated dose 90 day oral toxicity study (OECD TG 408) with the source substance vi.

0.1.2.1.3. Toxicity to reproduction or development

27 Test item related reproductive/developmental toxic effects are reported in

- a screening for reproductive/developmental toxicity study (OECD TG 422) with the Substance xi. (reductions in implantation index, delivery index, live birth index and birth index)
- a one generation reproductive toxicity study with the source substance vi. (litter losses in treated groups, mean litter size reduced)
- a prenatal developmental toxicity study with the source substance vi. (increase in pre-implantation loss and decreased litter size)
- a repeated dose 28-day oral toxicity study (OECD TG 407) conducted with the source substance vi. (increased ovarian follicle atresia and prolongation of the estrous stage)

0.1.2.1.4. Assessment outcome

28 The available set of data on the Substance and on the source substances indicates differences in the toxicological properties of the substances with potential hazardous effects on several end-points. This contradicts your read-across hypothesis whereby the Substance and source substances cause the same type of effect(s). However, you have not supported

and scientifically justified why such differences in the toxicological properties do not affect your read-across hypothesis.

0.1.2.2. Insufficient data density

29 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".

30 According to the Guidance on IRs and CSA, Section R.6.2.1.5., one of the factors in determining the robustness of a category is the density and distribution of the available data across the category. To identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the category members needs to be available.

31 You have provided:

- Skin sensitisation data obtained from the local lymph node assay (OECD TG 429) for one category member (the Substance, xi.);
- Bacterial reverse mutation test data for one category member (the Substance, xi.);
- In vitro cytogenicity data using the in vitro mammalian chromosomal aberration test (OECD TG 473) for one category member (the Substance xi.);
- In vitro gene mutation data obtained from the in vitro mammalian cell gene mutation test using the Hprt and Xprt genes (OECD TG 476) on category member (source substance vi.);
- Repeated dose 28-Day oral toxicity study data (OECD TG 407) for one category member (source substance vi.);
- Repeated dose 90 day oral toxicity study data (OECD TG 408) for one category member (source substance vi.);
- Data for screening for reproductive/developmental toxicity obtained from either a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422), or from an one-generation reproduction toxicity study (OECD TG 415) for two category members (the Substance xi., and source substance vi., respectively), and
- Prenatal developmental toxicity study data (OECD TG 414) for one category member (source substance vi.).

32 Based on these studies you claim that "*the available data show similarities and trends within the category in regard to… toxicological properties*", and that "*for those individual endpoints showing a trend, the pattern in the changing of potency is clearly and expectedly related to the carbon chain length of the dicarboxylic acid and the carbon chain length and/or branching of the alcohol*."

33 Information for one category member for skin sensitisation, one for 28-day and 90-day toxicity, one for bacterial reverse mutation test, one for in vitro cytogenicity, one for in vitro gene mutation, two for screening for reproductive/developmental toxicity, and one for developmental toxicity is not sufficient to establish a trend across the category consisting of 16 substances. Therefore, the information provided is not sufficient to conclude that toxicological properties are likely to follow a regular pattern.

0.1.2.1. Inadequate or unreliable studies on the source substance

34 According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

(1) be adequate for the purpose of classification and labelling and/or risk assessment;

(2) have adequate and reliable coverage of the key parameters addressed in the corresponding study that shall normally be performed for a particular information requirement;

(3) cover an exposure duration comparable to or longer than the corresponding study that shall normally be performed for a particular information requirement if exposure duration is a relevant parameter.

35 Specific reasons why the studies on the source substance(s) do not meet these criteria are explained further below under the applicable information requirement section 3. Therefore, no reliable predictions can be made for these information requirements.

0.1.3. Conclusion

36 Based on the 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 under Annex XI, Section 1.5. is rejected.

0.2. Weight of Evidence

37 Besides specifically claiming an adaptation using Annex XI, Section 1.5. (grouping of substances and read-across approach), you have indicated the adequacy of some of the endpoint study records as weight of evidence. Annex XI, section 1.2 (Weight of Evidence) requires that adequate and reliable documentation is provided to describe your weight of evidence approach. You have however not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/ assumption that the Substance has or has not a particular dangerous property. ECHA understands therefore you intend to adapt the information using Annex XI, Section 1.5. (grouping of substances and read-across approach) and has assessed the information on that basis.

Reasons related to the information under Annex VIII of REACH

1. In vitro gene mutation study in mammalian cells

38 An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII, Section 8.4.3., in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

1.1. Triggering of the information requirement

39 Your dossier contains negative results for both an Ames test and an *in vitro* cytogenicity study.

40 Therefore, the information requirement is triggered.

1.2. Information provided

41 You have adapted this information requirement by using Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from the following substances:

(i) an *in vitro* gene mutation study in mammalian cells (1988) with the source substance vi.

1.3. Assessment of the information provided

1.3.1. Read-across adaptation rejected

42 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

1.1. Study design

43 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.

2. Long-term toxicity testing on fish

44 Short-term toxicity testing on fish is an information requirement under Annex VIII, Column 1, Section 9.1.3. However, long-term toxicity testing on fish may be required by the Agency (Section 9.1.3., Column 2) if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

2.1. Triggering of the information requirement

45 In the provided reference to a publicly available document (OECD Screening Information Dataset (SIDS) Initial Assessment Profile)[2], the saturation concentration of the Substance in water was determined to be below the limit of detection of the analytical method (i.e. < 0.4 µg/L).

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

[2] Link to the OECD SIDS Initial Assessment Profile of Bis(2-ethylhexyl) azelate (i.e., the Substance): https://hpvchemicals.oecd.org/UI/handler.axd?id=4ed45505-d58f-4388-bb4f-36ea8b7c2e80

2.2. Information requirement not fulfilled

47 The information provided, its assessment and the specifications of the study design are addressed under request 5.

Reasons related to the information under Annex IX of REACH

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

48 A sub-chronic toxicity study (90 days) is an information requirement under Annex IX, Section 8.6.2.

3.1. Information provided

49 You have adapted this information requirement by using Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from the following substances:

(i) a sub-chronic toxicity study (1982) in the rat with the source substance vi.;

(ii) a sub-chronic toxicity study (1982) in the mouse with the source substance vi.;

(iii) a one-generation reproduction toxicity studies (1988) with the source substance vi.

3.2. Assessment of the information provided

3.2.1. Read-across adaptation rejected

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

3.2.1.1. Inadequate or unreliable studies on the source substance(s)

51 Under Annex XI, Section 1.5., the study to be read across must have an adequate and reliable coverage of the key parameters addressed/cover an exposure duration comparable to or longer than the one specified in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 408. Therefore, the following specifications must be met:

a) body weight and food consumption is measured at least weekly;

b) clinical signs are observed daily and functional observations (i.e. sensory activity, grip strength and motor activity assessments) are made during week 11 or later;

c) haematological and clinical biochemistry tests are performed as specified in paragraphs 30-38 of OECD TG 408

d) the oestrus cycle in females is examined at necropsy;

e) terminal organ and body weights are measured

f) gross pathological examinations as specified in paragraphs 43-46 of OECD TG 408

g) full histopathology is performed as specified in paragraphs 47-49 of OECD TG 408

h) the females should be nulliparous and non-pregnant.

52 In studies (i) and (ii):

a) there is no information on how frequently food consumption was measured;

b) functional observation battery was not assessed; In particular, the following investigations are missing: sensory reactivity to stimuli of different types (e.g. auditory, visual and proprioceptive stimuli), assessment of grip strength and motor activity assessment;

c) haematology and clinical biochemistry were not performed;

d) oestrus cyclicity was not assessed;

e) terminal organ weights were not assessed and thus and organ/body weight ratios were not recorded;

f) data of organs for which the pathological examination was perfomed is missing:

g) data of organs for which the histopathological examination was perfomed is missing.

In study (iii)

c) haematology and clinical biochemistry were not performed;

g) histopathology was performed on only on cervix, prostate, epididymis, seminal vesicle, liver, testis, mammary gland, uterus, ovary, abnormal tissues leaving out most of the tissues listed in in paragraphs 47-49 of OECD TG 408

h) the animals were mated and females gave birth to offspring after pregnancy.

53 The information provided does not cover the specifications required by the OECD TG 408.

54 Based on the above, the studies do not provide an adequate and reliable coverage of the key parameters specified in the OECD TG 408. Therefore these studies are not an adequate basis for your read-across predictions.

3.3. Study design

55 Following the criteria provided in Annex IX, Section 8.6.2., Column 2, and considering the Guidance on IRs and CSA, Section R.7.5.6.3.2., the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance.

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

57 Therefore, the study must be performed in rats according to the OECD TG 408 with oral administration of the Substance.

4. Pre-natal developmental toxicity study in one species

58 A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is an information requirement under Annex IX, Section 8.7.2.

4.1. Information provided

59 You have adapted this information requirement by using Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from the following substances:

(i) a pre-natal developmental toxicity study in rat (1988) with the source substance vi.

4.2. Assessment of the information provided

4.2.1. Read-across adaptation rejected

60 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

61 Therefore, the information requirement is not fulfilled.

4.3. Study design

62 A PNDT study according to the test method OECD TG 414 should be performed in rats or rabbits as preferred species.

63 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex IX, Section 8.7.2., Column 1).

64 Therefore, the study must be conducted in rats or rabbits with oral administration of the Substance.

5. Long-term toxicity testing on fish

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

5.1. Information provided

66 In the registration dossier, you have adapted this information requirement and provided the following justification:

(i) You refer to the PFAE linear category and claim that short-term aquatic toxicity test results indicate no potential for aquatic toxicity for category members with the exception of two water soluble substances (source substances i) and ii), as listed under Section 0.1 of this Decision). In addition to this, you note that the PFAE linear category includes no long-term toxicity to fish studies.

(ii) You mention that members of the PFAE linear category are readily biodegradable and on this basis you claim that exposure of aquatic organisms is unlikely.

(iii) You refer to the ECHA Guidance on IRs and CSA, Chapter R.7b (ECHA, 2012b) which states that "*chronic fish toxicity testing is generally only necessary, when the P and B criteria are fulfilled*" and claim that the Substance does not fulfil the P and B criteria.

(iv) You mention animal welfare.

67 In the comments to the draft decision, you have adapted this information requirement by using Annex XI, Section 1.3. (Qualitative or Quantitative Structure-Activity Relationships, (Q)SARs). To support the adaptation, you have provided the following information:

(i) predictions from ECOSAR v.2.2, Fish, ChV (Chronic Value) (2022) for the main constituent of the Substance (Nonanedioic acid, bis (2-ethylhexyl) ester, EC 203-091-7), and for the following identified impurities of the Substance:
- Octanedioic acid, bis (2-ethylhexyl) ester, CAS 5238-22-2;
- Decanedioic acid, bis (2-ethylhexyl) ester, EC 204-558-8;
- Undecanedioic acid, bis(2-ethylhexyl) ester, CAS 38717-66-7.

5.2. Assessment of information provided in the registration dossier

68 Regarding your justification under point (i), we have identified the following issue.

69 Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests do not give a true measure of toxicity for this type of substances and the long-term test is required. As explained above, under request 2, the Substance is poorly water soluble.

70 In addition to this, short-term fish studies (in this case, OECD TG 203 studies) cover different investigations than the ones that are needed to fulfil the long-term toxicity testing on fish information requirement (in this case, the investigations of OECD TG 210).

71 Because of these reasons, the finding that shows a lack of toxicity for a poorly water soluble substance in a short-term aquatic toxicity study cannot be used for excluding that the same substance will show measurable toxic effects in a long-term study.

72 As you have stated in your justification, the PFAE linear category includes no long-term toxicity to fish studies. Because of this, adapting the information requirement by referring to this category is not possible.

73 Regarding your justification under points (ii) and (iii), we have identified the following issue.

5.2.1. Your justification to omit the study has no legal basis

74 A registrant may only adapt this information requirement based on the general rules set out in Annex XI.

75 It is noted that Column 2 of Annex IX, Section 9.1, does not allow omitting the need to submit information on long-term toxicity to fish under Column 1.

76 Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH and the legal basis you are relying on for your intended adaptation is not apparent to ECHA.

77 Regarding your justification under point (iv), we have identified the following issue.

5.2.2. Your justification regarding minimisation of vertebrate testing is rejected

78 Minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI or Annex IX, Section 9.1., Column 2.

5.3. Assessment of information provided in the comments to the draft decision

5.3.1.1. Inadequate documentation of the prediction (QPRF)

79 Guidance on IRs and CSA 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.

80 You provided the following information about the prediction:

- the model prediction for fish Chronic Value (ChV);
- identification of the substances modelled, including their EC number, name and SMILES notation;

- your conclusion about the relationship between the modelled substance and the defined applicability domain: you report that the Substance is outside the applicability domain of the model.

81 The information you provided about the prediction lacks the following elements:

- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

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

5.4. Conclusion

83 Therefore, you have not demonstrated that this information can be omitted.

84 Therefore, the information requirement is not fulfilled.

5.5. Study design

85 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.).

86 The Substance is difficult to test due to the low water solubility (< 0.4 µg/L) and adsorptive properties: Log K_{ow} 9.59. OECD TG 210 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 210. 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.

87 In the comments to the draft decision, you indicate your intention to use passive dosing. You explain that you intend to use this approach, because you have found that other approaches (specifically, preparing the test solution using the Water Accomodated Franction approach and slow stirring) were not suitable for testing poorly water soluble substances that are similar to the Substance. In support of your claim, you mention the following specific difficulties: "*the substance will either not dissolve at all or it is not possible to generate reliable, reproducible and analytical detectable concentrations at the saturation limit as the substances tend to adsorb to filter, plastic, glassware and organisms*".

88 We acknowledge your intention to use passive dosing. As passive dosing is an approach included in OECD GD 23 among the approaches that are applicable for poorly water soluble substances, ECHA agrees that it is appropriate to consider its use for the requested study.

References

The following documents may have been cited in the decision.

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

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

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

Read-across assessment framework (RAAF)

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

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

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

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

Appendix 2: Procedure

The information requirement for an Extended One-Generation Reproductive Toxicity Study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. The EOGRTS may be addressed in a separate decision once the information from the sub-chronic toxicity study (90 days) requested in this decision is provided; because the results from the 90-day study are needed for the design of the EOGRTS. Similarly the information requirement for a screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) is not addressed in this decision; as the EOGRTS will cover the same parameters.

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 09 August 2022.

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

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

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.

In the comments to the draft decision, you requested an extension of the deadline to provide information from 36 months to 48 months from the date of adoption of the decision. You explained that additional time would be required to complete the testing due to 1) the long lead times at the in-house lab and at external contract research organizations which result in anticipated delays for conducting the long-term fish toxicity study, and 2) the work needed for the development and adaption of the passive dosing methodology in context of long-term toxicity to fish studies. You have not provided any documentary evidence to substantiate your request. On this basis, ECHA has not modified the deadline to provide information.

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

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

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

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

- the information specified in Annexe VII to REACH, for registration at 1-10 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, VIII, IX and X to REACH, for registration at >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 (https://echa.europa.eu/practical-guides).

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

1.2 Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

(1) Selection of the Test material(s)

The Test Material used to generate the new data must be selected taking into account the following:

- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/impurity on the test results for the endpoint to be assessed. For example, if a constituent/impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/impurity.

(2) Information on the Test Material needed in the updated dossier

- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include all constituents of each Test Material and their concentration values.

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers (https://echa.europa.eu/manuals).