~~Confidential~~

Helsinki, 15 August 2022

Addressees
Registrant(s) of JS_5343-92-0 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
03/08/2015

Registered substance subject to this decision ("the Substance")
Substance name: Pentane-1,2-diol
EC number: 226-285-3

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 ***25 May 2026***.

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. 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

3. Justification for an adaptation of a Screening for reproductive/developmental toxicity based on the results of the Extended one-generation reproductive toxicity study requested below (Annex VIII, Section 8.7.1.).

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

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 aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211);

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

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

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

8. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) by oral route, in rats, specified as follows:
   - Ten weeks premating exposure duration for the parental (P0) generation;
   - The highest dose level in P0 animals must be determined based on clear evidence of an adverse effect on sexual function and fertility without severe suffering or deaths in P0 animals as specified further in Appendix 1, or follow the limit dose concept. The reporting of the study must provide the justification for the setting of the dose levels;
   - Cohort 1A (Reproductive toxicity); and
   - Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation.

   You must report the study performed according to the above specifications. Any expansion of the study must be scientifically justified.

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.

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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 the read-across approach

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

- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.);
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.).

2 In addition, you have adapted the following standard information requirements under Column 2 of Annex X, Section 8.7:

- Pre-natal developmental toxicity study in a second species (Annex X, Section 8.7.2.);
- Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.).

3 These adaptations are supported solely by read-across information.

4 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.

5 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.

6 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. Predictions for toxicological properties

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

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

Source Substance 1	butane-1,2-diol, EC No. 209-527-2; and
Source Substance 2	hexane-1,2-diol, EC No. 230-029-6.

9 You provide the following reasoning for the prediction of toxicological properties: ”It is suggested that a read-across can be performed for toxicity endpoints based on the close structural similarity between pentane-1,2-diol, butane-1,2-diol and hexane-1,2-diol. As the functional groups of the target chemical are also present in the analogue substance, similar behavior in mammalian organisms can be expected.”

10 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.

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

0.1.1.1. Characterisation of the source substance(s)

12 Annex XI, Section 1.5 of the REACH Regulation provides that "substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as a group."

13 According to the Guidance on IRs and CSA, Section R.6, "the purity and impurity profiles of the substance and the structural analogue need to be assessed", and "the extent to which differences in the purity and impurities are likely to influence the overall toxicity needs to be addressed, and where technically possible, excluded". The purity profile and composition can influence the overall toxicity/properties of the Substance and of the source substance(s)(Guidance on IRs and CSA, Section R.6.2.3.1). Therefore, qualitative and quantitative information on the compositions of the Substance and of the source substance(s) must be provided to allow assessing whether the attempted predictions are compromised by the composition and/or impurities.

14 Your read-across justification document contains compositional information for the source substances. However, no information on the impurity profiles of the source substances is provided.

15 Without this information, no qualitative or quantitative comparative assessment of the compositions of the Substance and of the source substance(s) can be completed.

16 Therefore, it is not possible to assess whether the attempted predictions are compromised by the composition of the source substance(s).

0.1.1.2. Missing supporting information

17 Annex XI, Section 1.5 of the REACH Regulation states that "physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)". For this purpose "it is important to provide supporting information to strengthen the rationale for the read-across" (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.). The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

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

19 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).

20 For the source substances, you provide robust study summaries of the studies used for predicting the endpoints concerned, i.e. a pre-natal developmental toxicity study with Source Substance 2 and a reproductive / developmenatal toxicity screening study with Source Substance 1.

21 Apart from these studies with the source substances, your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data for the Substance itself that would confirm that the target substance and the source substances cause the same type of effects.

22 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.

0.1.1.3. Adequacy and reliability of source studies

23 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 test method referred to in Article 13(3);

(3) cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

24 Specific reasons why the studies on the source substance(s) do not meet these criteria are explained further below under the applicable information requirement sections:

- "Reasons related to the information under Annex VIII of REACH", see Section 3;
- "Reasons related to the information under Annex IX of REACH", see Section 4; and
- "Reasons related to the information under Annex X of REACH", see Section 8.

25 Therefore, no reliable predictions can be made for these information requirements.

26 On this basis your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

Reasons related to the information under Annex VII of REACH

1. In vitro gene mutation study in bacteria

27 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

28 You have provided an *in vitro* gene mutation study in bacteria conducted with the Substance (1993).

1.2. Assessment of the information provided

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

1.2.1. Study not adequate for the information requirement

30 To fulfil the information requirement, the study must meet the requirements of the OECD TG 471 (2020). Therefore, the following specifications must be:

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)

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

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

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

33 Therefore, the information requirement is not fulfilled.

1.3. Specification of the study design

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

2. Growth inhibition study aquatic plants

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

2.1. Information provided

36 You have provided a study according to DIN 38412 part 9 on the Substance.

2.2. Assessment of the information provided

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

2.2.1. The provided study does not meet the information requirement

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

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

39 Reporting of the methodology and results

b) the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported. Algal biomass is normally determined based on dry weight per volume, or alternatively as cell counts or biovolume using microscopy or an electric particle counter. If an alternative method is used (*e.g.* flow cytometry, *in vitro* or *in vivo* fluorescence, or optical density), a satisfactory correlation with biomass must be demonstrated over the range of biomass occurring in the test;

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

40 Validity criteria

d) the following criteria must be met:

- exponential growth in the control cultures is observed over the entire duration of the test;
- at least 16-fold increase in biomass is observed in the control cultures by the end of the test;
- the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%;
- the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures is ≤ 7% in tests with *Desmodesmus subspicatus*.

41 Your registration dossier provides a study according to the DIN 38412 part 9. You have provided further information in your comments to the draft decision where you disagree to perform a new study as requested in this decision. Taken together, the information provided shows the following:

42 Reporting of the methodology and results

a) you report that algal biomass was determined using fluorometry. However, you have not reported evidence of correlation between the measured parameter and dry weight or cell numbers over the range of biomass occurring in the test. In the comments to the draft decision you indicate that this information is available. However, you do not provide this information. Instead, you only provide the percentage of growth inhibition after 72 hours, based on growth rate and biomass;

b) tabulated data on the algal biomass determined daily for each treatment group and control are not reported. In the comments to the draft decision you indicate that this information is available. However, you do not provide it;

43 Validity criteria

c) you have not provided data on the control cultures allowing independent assessment of the validity criteria.

44 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results.

45 More specifically, , the reporting of the study is not sufficient to conduct an independent assessment of its reliability.

46 More specifically, you have provided tabulated data on the average fluorescence determined in tested concentration however you have not reported the measurements for each control replicate nor the correlation between the reported fluorescence values and cell biomass.

47 In the comments to the draft decision the information is claimed to be available. However the information was not attached to the comments. Hence, it is not possible to perform an independent assessment of the study validity.

48 Based on the above, the requirements of the OECD TG 201 are not met. On this basis, the information requirement is not fulfilled.

Reasons related to the information under Annex VIII of REACH

3. Screening for reproductive/developmental toxicity

49 Screening for reproductive/developmental toxicity is a standard information requirement under Annex VIII to REACH. This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 of Annex VIII or a general adaptation rule under Annex XI.

3.1. Information provided

50 You have adapted this information requirement by using a Grouping of substances and read-across approach based on experimental data from the following substances:

(i) Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (1994) conducted with the Source Substance 1.

3.2. Assessment of the information provided

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

3.2.1. Read-across adaptation rejected

52 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.

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

3.2.1. Source study not adequate for the information requirement

54 Under Annex XI, Section 1.5., the study to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case the OECD TG 421. Therefore, the following specifications must be met:

a. at least 10 male and 12-13 female animals for each dose and control group;
b. an exposure duration of at least four weeks for males, including a minimum of two weeks prior to mating, and approx. 63 days for females to cover premating, conception, pregnancy and at least 13 days of lactation;
c. at least weekly body weight and food consumption measurements;
d. at least weekly food consumption measurements;
e. nature, severity, and duration of clinical signs observed daily;
f. terminal organ and body weights;
g. gross pathology, including incidence and severity, as specified in paragraphs 45-48 of OECD TG 421;
h. full histopathology, including incidence and severity, as specified in paragraph 49 of OECD TG 421.

55 The study (i) is described as a Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test. However, the following specifications are not according to the requirements of OECD TG 421:

a. only 10 female animals in each dose and control group;

b. an exposure duration of only 3 days of lactation for females;
c. data on body weights, body weight changes and food consumption is missing;
d. data on food consumption is missing;
e. data on clinical signs is missing;
f. data on terminal organ weights and organ/body weight ratios is missing;
g. data on gross pathology findings: incidence and severity is missing;
h. data on histopathology findings: incidence and severity is missing.

56 For points (c.-h.) you have not provided any methodological description and instead given a single sentence under each methodological subsection: "*Study design was stated to be in line with Guideline OECD 422*." For the results section you have provided only a single paragraph in which you claim that no effects were observed in any parameters. The lack of detailed description and numerical data precludes an independent assessment of the claimed no effects.

57 Based on the above, the study does not provide an adequate and reliable coverage of the key parameters addressed by the OECD TG 421 and this study is not an adequate basis for your read-across predictions.

3.3. Specification of the study design

58 The present decision requests the registrants concerned to generate and submit an extended one-generation reproductive toxicity study (EOGRTS) (see Section 8 below). Once an EOGRTS is available, according to Column 2 of Annex VIII, Section 8.7.1. and in order to prevent unnecessary animal testing, a screening for reproductive/developmental toxicity does not need to be conducted. While you still have to comply with the information requirement in Annex VIII, Section 8.7.1., you are requested to submit a justification for the adaptation based on Column 2 of that provision.

Reasons related to the information under Annex IX of REACH

4. Pre-natal developmental toxicity study in one species

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

4.1. Information provided

60 You have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data:

(ii) Pre-natal Developmental Toxicity study (2006) conducted with the Source Substance 2.

4.2. Assessment of the information provided

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

4.2.1. Read-across adaptation rejected

62 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.

63 On this basis, the information requirement is not fulfilled

4.2.2. Source study not adequate for the information requirement

64 Under Annex XI, Section 1.5., the study to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case the OECD TG 414. Therefore, the following specifications must be met:

a. body weight and food consumption measurements at least every three days;

b. nature, severity, and duration of clinical signs observed daily;

c. examination of the dams for any structural abnormalities, weight and histopathology of the thyroid gland, thyroid hormone measurements, gravid uterus weight, and uterine content.

d. examination of the foetuses for body weight, number and percent of live and dead foetuses and resorptions, sex ratio, external, skeletal and soft tissue alterations (variations and malformations), measurement of anogenital distance in all live rodent foetuses.

65 The study (i) is described as a Pre-natal developmental toxicity study. However, the following specifications are not according to the requirements of OECD TG 414:

a. no data on body weights, body weight changes and food consumption.

b. no information on clinical signs: nature and severity.

c. no data on examinations of dams: incidence and severity.

d. no data on examinations of foetuses: incidence and severity.

66 For points (a.-c.) you have provided a single sentence "Maternal toxic effects:no effects" and for the point (d.) you have provided a single sentence "Embryotoxic / teratogenic effects:no effects". The lack of detailed description and numerical data precludes an independent assessment of the claimed no effects.

67 Based on the above, the study does not provide an adequate and reliable coverage of the key parameters addressed by the OECD TG 414 and this study is not an adequate basis for your read-across predictions.

4.3. Specification of the study design

68 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species.

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

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

5. Long-term toxicity testing on aquatic invertebrates

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

5.1. Information provided

72 A) In your dossier, you have provided a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2.

73 In support of your adaptation, you provided the following justification: *"In Annex IX of Regulation (EC) No 1907/2006, it is laid down that long-term toxicity testing shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on aquatic organisms. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or is assessed to be a PBT or vPvB. The hazard assessment of pentane-1,2 -diol reveals neither a need to classify the substance as dangerous for the environment, nor is it a PBT or vPvB substance. Therefore a long-term toxicity study in aquatic invertebrates is not provided*".

74 B) In your comments to the draft decision you do not agree to perform the requested study. Instead, you indicate your intention to adapt the following standard information requirements by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2. To support your adaptation, ECHA understands you have sought to use the following information on the Substance:

(i) study according to OECD TG 203

(ii) study according to EU Directive 79/831/EWG Appendix V, part C

(iii) study according to DIN 38412 part 9

(iv) QSAR Toolbox 4.4 to predict long-term toxicity to fish, reporting NOEC value based on mortality

(v) QSAR Toolbox 4.4 to predict long-term toxicity to aquatic invertebrates, reporting NOEC value based on reproduction

(vi) expert judgement referring to the additional following information:

a. readily biodegradability property of the Substance

b. prediction pointing to no protein binding capacity, as "an indication of the absence of elevated toxicity"

c. prediction showing the Substance to be a neutral organic of class 1 (narcosis or baseline toxicity], to support that "critical long-term effects are not to be expected"

d. With regards to PBT assessment, the Substance is neither P/vP nor B/vB and "holds no relevant classification"

e. Properties of the Substance (e.g. water solubility, low adsorption and low volatility) to support substance stability under test conditions

5.2. Assessment of the information provided

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

76 A) with regards to the proposed adaptation under Annex IX, Section 9.1., Column 2 provided in your dossier we remark the following:

5.2.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study

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

78 Your adaptation is therefore rejected.

79 B) with regards to the adaptation under Annex XI, Section 1.2 provided in your comments to the draft decision:

5.2.2. Annex XI, Section 1.2 is rejected

80 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.

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

82 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude on the corresponding information requirement.

83 Relevant information that can be used to support weight of evidence adaptation for the information requirement of Annex IX, Section 9.1.5 includes similar information that is produced by the OECD TG 211. OECD TG 211 requires the study to investigate the concentrations of the test material leading to no observed effect (NOECs) on the following key parameters:

1) the reproductive output of Daphnia sp. expressed as the total number

of living offspring produced at the end of the test, and
2) the survival of the parent animals during the test, and
3) the time to production of the first brood.

1. *Key parameters 2 and 3*
2. None of the sources of information (i) to (vi) provide relevant information on survival of the parental animals and the time of production of the first brood.*Key parameter 1*

84 Sources of information (i) to (iv) and (vi) do not provide relevant information on the reproductive output of Daphnia sp..

85 Source of information (v) does provide relevant information on this key paramenter.

86 However, the reliability of source of information (v) is significantly affected by the following deficiencies:

5.2.2.1. Inappropriate measures of robustness of the model

87 Under Guidance on IRs and CSA, Section R.6.1.3., a (Q)SAR model must fulfil the principles described in the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) to be considered scientifically valid. For that purpose, the fourth OECD principle requires that a model has appropriate measures of the internal performance (i.e. goodness-of-fit and robustness) and predictivity.

88 You use a Toolbox profiler to make a prediction for the endpoint without measures of internal performance and predictivity of the profiler for the prediction of this endpoint.

89 Calculation of confidence intervals may show substances with large difference between observed and calculated toxicity. A new trend analysis might have better statistical parameters and refined slope and intercept calculated in the quantitative relationship.

90 You have excluded 35 values for 18 chemicals from the relationship due to inconsistency. However, you have not provided explanation regarding this removal. In absence of any justification, you have not established the scientific validity of the model.

5.2.2.2. Inadequate documentation of the model (QMRF)

91 Under Appendix C of the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) and Guidance on IRs and CSA 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.

92 Data on analogues, experimental test results and data aggregation that have been used to build the trend analyses (model) are missing. When data aggregation is performed, it should be analysed for extreme values and these should be discussed.

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

5.2.2.3. Inadequate documentation of the prediction (QPRF)

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

95 The reliability of the endpoint information (experimental data) and the suitability of analogues that has been used to build the trend analyses (model) and calculate the prediction cannot be assessed, since the prediction reports were not associated with data matrix.

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

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

98 In summary, none of the sources of information (i) to (vi) provide relevant information on key parameters 2 and 3 listed above. The source of information (v) provides relevant information on the reproductive output of Daphnia sp. However, source of information (v) has significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for long-term toxicity to aquatic invertebrates.

99 Hence, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for long-term toxicity to aquatic invertebrates. Therefore, your adaptation is rejected.On this basis, the information requirement is not fulfilled.

6. Long-term toxicity testing on fish

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

6.1. Information provided

101 A) in your dossier, you have provided a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2.

102 In support of your adaptation, you did not provide a justification/provided the following justification: "*In Annex IX of Regulation (EC) No 1907/2006, it is laid down that long-term toxicity testing shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on aquatic organisms. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or is assessed to be a PBT or vPvB. The hazard assessment of pentane-1,2-diol reveals neither a need to classify the substance as dangerous for the environment, nor is it a PBT or vPvB substance. Therefore, and for reasons of animal welfare, a long-term toxicity study in fish is not provided*".

103 B) In your comments to the draft decision you do not agree to perform the requested study. Instead, you indicate your intention to adapt the following standard information requirements by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2. To support your adaptation, ECHA understands you have sought to use the following information:

(i) study according to OECD TG 203

(ii) study according to EU Directive 79/831/EWG Appendix V, part C

(iii) study according to DIN 38412 part 9

(iv) QSAR Toolbox 4.4 to predict long-term toxicity to fish, reporting NOEC value based on mortality

(v) QSAR Toolbox 4.4 to predict long-term toxicity to aquatic invertebrates, reporting NOEC value based on reproduction

(vi) expert judgement referring to the additional following information:

a. readily biodegradability property of the Substance

b. prediction pointing to no protein binding capacity, as "an indication of the absence of elevated toxicity"

c. prediction showing the Substance to be a neutral organic of class 1 (narcosis or baseline toxicity], to support that "critical long-term effects are not to be expected"

d. With regards to PBT assessment, the Substance is neither P/vP nor B/vB and "holds no relevant classification"

e. Properties of the Substance (e.g. water solubility, low adsorption and low volatility) to support substance stability under test conditions

f. Animal welfare reasons

6.2. Assessment of the information provided

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

105 A) with regards to the proposed adaptation under Annex IX, Section 9.1., Column 2 provided in your dossier we remark the following:

6.2.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study

106 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).

107 Your adaptation is therefore rejected.

108 B) with regards to the adaptation provided in your comments to the draft decision:

6.2.2. Annex XI, Section 1.2 is rejected

109 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.

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

111 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude on the corresponding information requirement.

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

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

Key parameter 1, 3 and 4

113 None of the sources of information (i) to (vi) provide relevant information on the embryonic development, the appearance and behavior of larvae and juvenile fish and the weight and length of the fish.

Key parameter 2

114 Sources of information (i), (ii), (iii), (v) and (vi) do not provide relevant information on the hatching of fertilized eggs and survival of embryos, larvae and juvenile fish.

115 Source of information (iv) does provide limited relevant information on this key parameter as the reported values are based on fish mortality, i.e. it addresses survival of juvenile fish.

116 However, the reliability of source of information (iv) is significantly affected by the following deficiency:

6.2.2.1. Inappropriate measures of robustness of the model

117 Under Guidance on IRs and CSA, Section R.6.1.3., a (Q)SAR model must fulfil the principles described in the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) to be considered scientifically valid. For that purpose, the fourth OECD principle requires that a model has appropriate measures of the internal performance (i.e. goodness-of-fit and robustness) and predictivity.

118 You use a Toolbox profiler to make a prediction for the endpoint without measures of internal performance and predictivity of the profiler for the prediction of this endpoint.

119 Calculation of confidence intervals may show substances with large difference between observed and calculated toxicity. You may have also a substance with large leverage. A new trend analysis might have better statistical parameters and refined slope and intercept calculated in the quantitative relationship.

120 You have excluded a total of 8 values for 3 chemicals from the relationship due to inconsistency. However, you have not provided explanation regarding this removal. In absence of any justification, you have not established the scientific validity of the model.

6.2.2.2. Inadequate documentation of the model (QMRF)

121 Under Appendix C of the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) and Guidance on IRs and CSA 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;

122 Data on analogues, experimental test results and data aggregation that have been used to build the trend analyses (model) are missing. When data aggregation is performed, it should be analysed for extreme values and these should be discussed.

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

6.2.2.3. Inadequate documentation of the prediction (QPRF)

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

125 The reliability of the endpoint information (experimental data) and the suitability of analogues that has been used to build the trend analyses (model) and calculate the prediction cannot be assessed, since the prediction reports were not associated with the data matrix.

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

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

128 In summary, none of the sources of information (i) to (vi) provide relevant information on the key parameter 1, 3 and 4 listed above. The source of information (iv) provides relevant information on the survival of juvenile fish. However, this source of information (iv) has significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for long-term toxicity to fish.

129 Hence, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for long-term toxicity to fish. Therefore, your adaptation is rejected.It is also noted that minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI.

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

6.3. Test specifications

131 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.).

Reasons related to the information under Annex X of REACH

7. Pre-natal developmental toxicity study in a second species

132 Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is an information requirement under Annex X to REACH (Section 8.7.2.).

7.1. Information provided

133 You have adapted this information requirement by using an adaptation in accordance with Column 2 of Annex X, Section 8.7. To support the adaptation, you have provided following information:

134 You claim that the overall toxicity of the Substance is low. You support this statement by reading across to reproductive/developmental screening test conducted with Source Substance 1 and a pre-natal development study conducted with Source Substance 2.

7.2. Assessment of the information provided

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

7.2.1. Column 2 adaptation rejected

136 Under Section 8.7., column 2 of Annex IX to REACH, the study does not need to be conducted if the substance is of low toxicological activity. This needs to be demonstrated with three concomitant criteria:

- that there is no evidence of toxicity seen in any of the tests available;
- that it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure; and
- that there is no or no significant human exposure.

137 You have provided a read-across screening study from the Source Substance 1 and a read-across pre-natal development study from the Source Substance 2 to support your low toxicity claim.

138 As explained in section 0.1 your read-across approach is rejected. Therefore the information provided (read-across screening study from the Source Substance 1 and a read-across pre-natal development study from the Source Substance 2) is not relevant to support your claim of low toxicity.

139 You have not provided any toxicokinetic data demonstrating no systemic absorption occurs following exposure to the Substance.

140 The use and exposure information indicates widespread use by professional workers which include: PROC 8a: Transfer of substance or mixture (charging and discharging) at non-dedicated facilities; PROC 10: Roller application or brushing; PROC 11: Non-industrial spraying; and PROC 13: Treatment of articles by dipping and pouring.

141 In addition, the Substance has consumer uses in washing and cleaning products and air care products.

142 You have provided no proof that the Substance is not absorbed following oral and inhalation exposure. The uses of the Substance indicate that here is significant human exposure.

143 ECHA concludes that the above mentioned criteria for demonstrating low toxicological activity are not met. Therefore, your adaptation is rejected.

144 Based on the above, the information you provided does not fulfil the information requirement.

7.3. Specification of the study design

145 A PNDT study according to the OECD TG 414 study should be performed in the rabbit or rat as the preferred second species, depending on the species tested in the first PNDT study.

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

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

8. Extended one-generation reproductive toxicity study

148 An extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is an information requirement under Annex X to REACH (Section 8.7.3.).

8.1. Information provided

149 You have adapted this information requirement by using an adaptation in accordance with Column 2 of Annex X, Section 8.7. To support the adaptation, you have provided following information:

150 You claim that the overall toxicity of the Substance is low. You support this statement by reading across to reproductive/developmental screening test conducted with Source Substance 1 and a pre-natal development study conducted with Source Substance 2.

8.2. *Assessment of the information provided*

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

8.2.1. Column 2 adaptation rejected

152 Your adaptation based on Column 2 of Annex X, Section 8.7 is rejected for the reasons set out under Section 6.2.1 of this decision which equally apply to the information you provided for this information requirement.

153 Based on the above, the information you provided does not fulfil the information requirement.

8.3. Specification of the study design

8.3.1. Species and route selection

154 A study according to the test method OECD TG 443 must be performed in rats with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

8.3.2. Pre-mating exposure duration

155 The length of pre-mating exposure period must be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

156 Ten weeks pre-mating exposure duration is required to obtain results adequate for classification and labelling and/or risk assessment. There is no substance specific

information in the dossier supporting shorter premating exposure duration (Guidance on IRs and CSA, Section R.7.6.).

157 In the comments to the draft decision you disagree with the request of ten weeks pre-mating exposure duration. You consider that in light of the available data, a two-week pre-mating exposure duration is sufficient. You state that a request for ten weeks is not in line with the REACH information requirement (Annex X, Section 8.7.3), OECD TG 443, OECD GD 151 or REACH Article 25, and such a request requires a scientific justification from ECHA. Finally, you consider that the ECHA Guidance documents are not legally binding and therefore they do not overrule the legal text or the test guideline requirements.

158 ECHA notes that REACH Annex X, Section 8.7.3 does not address premating exposure duration. ECHA acknowledges that OECD TG 443 and GD 151 state that in most cases, a two-week premating exposure is sufficient, however it can be adapted when justified. ECHA agrees that the available data does not show impairment of spermatogenesis or effects on oestrous cycle (cf. OECD TG 443, para 28). However, ECHA notes that the available OECD TG 422 and 408 studies provide limited information with regard to mating and fertility. The OECD TG 422 study has a two-week pre-mating exposure duration not covering the full spermatogenesis and folliculogenesis, whereas the exposure in the OECD TG 408 study is twelve weeks with no information on mating. In addition, the statistical power is low in these studies compared to EOGRTS.

159 ECHA highlights that the EOGRT study should fulfil regulatory requirements and be capable of providing information on fertility that is adequate for example for hazard identification and risk assessment as well as classification and labelling, including categorisation (OECD TG 443, paragraph 22). For these purposes, the ten weeks premating exposure duration is one of the elements together with the appropriate dose level selection which allow production of data for an informed decision making for classification and labelling, including categorisation, for the hazard endpoint for sexual function and fertility, and for risk assessment.

160 A ten weeks pre-mating exposure duration covers the full spermatogenesis and maturation meaning that the full cycle of development of sperm from spermatogonia into mature sperm is exposed. Thus, ten weeks premating exposure duration allows an assessment of the adverse effects on fertility by combining the information from all possible parameters in males evaluated at the same time. Similarly, the folliculogenesis is fully covered only after a long exposure period, such as ten weeks. It is important to expose all the developmental stages of the sperm and follicles before the mating in order to be able to evaluate any potential adverse effect on fertility.

161 If the premating exposure is only two weeks, this exposure duration does not cover the full cycle of gamete production and therefore possible fertility effects resulting from effects of the Substance on the whole cycle of gamete production can be missed. Therefore, such study would be considered inconclusive for such effects for classification and labelling purposes.

162 With regard to animal welfare, you consider that a longer pre-mating exposure duration would be linked to animal pain and stress without producing any additional information. As explained above, the ten weeks pre-mating exposure duration allows production of data for an informed decision making.

163 The information provided in your comments does not change the assessment.

164 Therefore, the requested pre-mating exposure duration is ten weeks.

8.3.3. Dose-level setting

165 The aim of the requested test must be to demonstrate whether the classification criteria of the most severe hazard category for sexual function and fertility (Repr. 1B; H360F) and developmental toxicity (Repr. 1B; H360D) under the CLP Regulation apply for the Substance (OECD TG 443, para. 22; OECD GD 151, para. 28; Annex I Section 1.0.1. of REACH and Recital 7, Regulation 2015/282), and whether the Substance meets the criteria for a Substance of very high concern regarding endocrine disruption according to Art.57(f) of REACH as well as supporting the identification of appropriate risk management measures in the chemical safety assessment.

166 To investigate the properties of the Substance for these purposes, the highest dose level must be set on the basis of clear evidence of an adverse effect on sexual function and fertility, but no deaths (i.e., no more than 10% mortality; Section 3.7.2.4.4 of Annex I to the CLP Regulation) or severe suffering such as persistent pain and distress (OECD GD 19, para. 18) in the P0 animals.

167 In case there are no clear evidence of an adverse effect on sexual function and fertility, the limit dose of at least 1000 mg/kg bw/day or the highest possible dose level not causing severe suffering or deaths in P0 must be used as the highest dose level. A descending sequence of dose levels should be selected to demonstrate any dose-related effect and aiming to establish the lowest dose level as a NOAEL.

168 In summary: Unless limited by the physical/chemical nature of the Substance, the highest dose level in P0 animals must be as follows:

(1) in case of clear evidence of an adverse effect on sexual function and fertility without severe suffering or deaths in P0 animals, the highest dose level in P0 animals must be determined based on such clear evidence, or
(2) (2 in the absence of such clear evidence, the highest dose level in P0 animals must be set to be the highest possible dose not causing severe suffering or death, or
(3) if there is such clear evidence but the highest dose level set on that basis would cause severe suffering or death, the highest dose level in P0 animals must be set to be the highest possible dose not causing severe suffering or death, or
(4) the highest dose level in P0 animals must follow the limit dose concept.

169 You have to provide a justification with your study results demonstrating that the dose level selection meets the conditions described above.

170 Numerical results (i.e. incidences and magnitudes) and description of the severity of effects at all dose levels from the dose range-finding study/ies must be reported to facilitate the assessment of the dose level section and interpretation of the results of the main study.

8.3.4. Cohorts 1A and 1B

171 Cohorts 1A and 1B belong to the basic study design and must be included.

172 Histopathological investigations in Cohorts 1A and 1B:

173 In addition to histopathological investigations of cohorts 1A, organs and tissues of Cohort 1B animals processed to block stage, including those of identified target organs, must be subjected to histopathological investigations (according to OECD TG 443, para. 67 and 72) if:

- the results from Cohort 1A are equivocal,
- the test substance is a suspected reproductive toxicant or
- the test substance is a suspected endocrine toxicant.

174 Splenic lymphocyte subpopulation analysis:

175 Splenic lymphocyte subpopulation analysis must be conducted in Cohort 1A (OECD TG 443, para. 66; OECD GD 151, Annex Table 1.3).

176 Investigations of sexual maturation:

177 To improve the ability to detect rare or low-incidence effects, all F1 animals must be maintained until sexual maturation to ensure that sufficient animals (3/sex/litter/dose) are available for evaluation of balano-preputial separation or vaginal patency (OECD GD 151, para. 12 in conjunction with OECD TG 443, para. 47). For statistical analyses, data on sexual maturation from all evaluated animals/sex/dose must be combined to maximise the statistical power of the study.

8.4. Further expansion of the study design

178 The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if relevant information becomes available from other studies or during conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Column 2, Section 8.7.3., Annex X. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in Guidance on IRs & CSA, Section R.7.6.

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 08 June 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) and the deadline.

Deadline to submit the requested information in this decision

You requested an extension of the deadline from 30 months specified in the decision to 48 months. You claim that the extension is needed for the possible delays because of limited capacity in the Contract Research Organizations (CRO), and also because it will be necessary to conduct further range finding studies for proper dose selection in the requested main studies.

ECHA acknowledges the explanation you have provided about CRO capacity, however you have not provided any documentary evidence to substantiate your request based on the limited capacity in the CRO. Furthermore, ECHA notes that the deadline is provided to perform the requested experimental studies including the dose range finding studies for the dose level selection.

On this basis, ECHA has not modified the deadline to provide the 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.

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. This is independent of the extension of the deadline you requested in the comments to the draft decision, which at the time was not substantiated by documentary evidence, as explained above.

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]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
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[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