~~Confidential~~

Helsinki, 20 June 2023

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

Date of submission of the dossier subject to this decision
16/12/2020

Registered substance subject to this decision ("the Substance")
Substance name: Phthalic acid
EC/List number: 201-873-2

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***5 January 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. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202)

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

3. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: EU C.4. A/B/C/D/E/F/OECD TG 301A/B/C/D/E/F or EU C.29./OECD TG 310)

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

4. Justification for an adaptation of the Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1. column 2) based on the request for an extended one-generation reproductive toxicity study in decision TPE-D-2114643515-49-01/F.

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

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

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

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

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

The reasons for the decision(s) are explained in Appendix 1.

Information required depends on your tonnage band

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

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report, where** relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

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

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

Appendix 1: Reasons for the request(s)

Contents

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.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2)
- Long-term toxicity testing on fish (Annex VIII, Section 9.1.3, column 2)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

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. Predictions for (eco)toxicological properties

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

6 You predict the properties of the Substance from information obtained from the following source substance:

- PA: phthalic anhydride with EC no. 201-607-5
- HPP: Hydrogen potassium phthalate EC no. 212-889-4

7 You provide the following reasoning for the prediction of (eco)toxicological and environmental fate properties: "Phthalic anhydride hydrolyses rapidly in the presence of water forming phthalic acid. The kinetic of the hydrolysis of phthalic anhydride was studied to be 30.5 seconds at pH 7.24 and 25 °C, 52.5 seconds at pH 6.8 and 75 (66.6 to 79.5) seconds at pH 0 to 6 and 25°C" .

8 ECHA understands that your read-across hypothesis is based on the formation of common (bio)transformation products. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

9 We have identified the following issue with the predictions of (eco)toxicological and environmental fate properties:

0.1.1.1. Inadequate or unreliable studies on the source substance

10 According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must have adequate and reliable coverage of the key parameters addressed in the corresponding study that shall normally be performed for a particular information requirement.

11 Specific reasons why the studies on the source substance do not meet these criteria are explained further below under the applicable information requirements in sections 3 to 5 and 7 to 8. Therefore, no reliable predictions can be made for these information requirements.

0.1.2. Conclusion on the read-across approach

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

Reasons related to the information under Annex VII of REACH

1. Short-term toxicity testing on aquatic invertebrates

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

1.1. Information provided

14 You have provided the following information on the Substance:

(i) a short-term toxicity study on *Daphnia magna* (1986) according to U.S. EPA (1975) EPA 660/3-75-009

(ii) a non guideline short-term toxicity study on aquatic invertebrates (1980)

1.2. Assessment of the information provided

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

15 To fulfil the information requirement, a study must comply with OECD TG 202 (Article 13(3) of REACH).

16 Therefore, the following specifications must be met:

17 Technical specifications impacting the sensitivity/reliability of the test

a) *Daphnia magna* (or other suitable Daphnia species) is used as test species;

18 Characterisation of exposure

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

19 Reporting of the methodology and results:

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

20 In study (i) described as short-term toxicity study on daphnia magna:

21 Characterisation of exposure

b) No analytical monitoring of exposure was conducted.

In the comment to the draft decision, you confirm that no analytical monitoring was performed. However, you argue that the Substance is stable and the algae study provide evidence that the concentration of the test substance can be satisfactorily maintained within ± 20 % of the nominal or measured initial concentration throughout the test. However, stable exposure in a given study is not a direct proof that exposure was statisfactory in the target study unless you can demonstrate that difference in exposure conditions have no impact and that exposure at the beginning of the test in the target study was consistent with nominal concentrations. You have provided no such justification.

22 Reporting of the methodology and results.

c) You did not report the number of immobilised daphnids determined at 24 and 48 hours.

In your comment to the draft decision, you provide the missing information.

23 In study (ii) described as short-term toxicity study on aquatic invertebrate:

24 Technical specifications impacting the sensitivity/reliability of the test

a) the test was conducted on the non-standard organism *Chironomus plumosus*.

25 Characterisation of exposure

b) No analytical monitoring of exposure was conducted. The comments provided by you on study (i) and ECHA's reply equally applies to study (ii).

26 Reporting of the methodology and results:

c) You did not report the number of immobilised test animals determined at 24 and 48 hours.

27 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically
  - as no analytical monitoring of exposure was conducted for studies (i) and (ii), you have not demonstrated that exposure was satisfactorily maintained in this test and that effect concentrations can be expressed based on nominal concentrations in the studies;
  - in study (ii), a non-standard test organism is used and consequently the key parameter of the OECD TG 202 is not covered;
- the reporting of study (ii) is not sufficient to conduct an independent assessment of its reliability. In the absence of tabulated results, it is not possible to conduct an independent assessment of these studies. You have provided the missing information for study (i) in your comments. However, as the information is currently not available in your registration dossier, the identified issue remains.

28 Therefore, the requirements of OECD TG 202 are not met in any of the provided studies and this information requirement is not fulfilled.

29 In your comments on the draft decision, you also explain that, instead of performing a new OECD TG 202 study as requested, you propose to adapt the information requirement by using Annex VII, section 9.1.1., column 2.

30 Should you decide to pursue your intended adaptation, ECHA bring your attention to the following observations. REACH Annex VII, section 9.1.1., column 2 specifies that the short-term toxicity study does not need to be conducted if a long-term aquatic toxicity study on invertebrates is available. At present no long-term toxicity study on aquatic invertebrates is provided in the IUCLID dossier, therefore no conclusion on the compliance can currently be made. In any case, you remain responsible for complying with this decision by the set deadline.

2. Growth inhibition study aquatic plants

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

2.1. Information provided

32 You have provided a Growth inhibition study on algae (2004) with the Substance according to EU Method C.3.

2.2. Assessment of the information provided

2.2.1. The provided study does not meet the specifications of the test guideline

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

34 Reporting of the methodology and results

a) the test design is reported (*e.g.*, number of replicates).
b) the test conditions are reported (*e.g.*, composition of the test medium, test temperature).
c) 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.
d) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

35 In the provided study described as growth inhibition study on algae:

36 Reporting of the methodology and results

a) on the test design, you have not specified in your dossier the number of replicates. In the comment to the draft decision, you provide information that the study (i) was performed in triplicates.

b) on the test conditions, you have not specified in your dossier the test temperature and the composition of the test medium (including the nature of the buffer used for pH adjustment). In the comments to the draft decision, you provide a full study report which includes the missing information.

c) you have not specified in your dossier the method used to determine algal biomass and, if relevant, that the method allows adequate quantification of biomass. In the comments to the draft decision, you state that cell density measurements are made using a microcell counter or, alternatively, are determined by means of a microscopic counting chamber.

d) the results of algal biomass determined in each flask at least daily during the test period are not reported in your dossier. In the comments to the draft decision, you provide a full study report which includes the missing information.

37 Based on the above, the reporting of the study as currently reported in your dossier is not sufficient to conduct an independent assessment of its reliability.

38 In the comments to the draft decision, you provide missing information and adequately addressed the issues identified above under points a) to d).

39 ECHA acknowledges that based on this additional information in your comments, the study could meet the information requirement. However, as the information is currently not available in your registration dossier, the data gap remains. You must therefore submit this information in an updated registration dossier by the deadline set out in the decision.

3. Ready biodegradability

40 Ready biodegradability is an information requirement in Annex VII to REACH (Section 9.2.1.1.).

3.1. Information provided

41 You have provided the following information on the Substance:

(i) a ready biodegradability study (1973) according to OECD TG 301D;

(ii) an inherent biodegradability study (1980) according to EU Method C.9;

(iii) a ready biodegradability study (1992) according to OECD TG 301C with the analogue Phthalic anhydride (EC no. 201-607-9);

42 In your comment to the draft decision, you provided the following additional information:

(iv) a ready biodegradability study (2018), performed according to the OECD TG 301D with the source substance Hydrogen potassium phthalate (EC no. 212-889-4);

(v) a ready biodegradability study (1976), performed according to the OECD TG 301C with the source substance Phthalic anhydride (EC no. 201-607-9);

(vi) a QSAR prediction from BIOWIN (v.4.11), 2022;

(vii) a QSAR prediction from VEGA (v.1.1.5), 2022.

3.2. Assessment of the information provided

3.2.1. Assessment of the information provided on the Substance

3.2.1.1. The study (i) does not meet the specifications of the test guideline

43 To fulfil the information requirement, a study must comply with the OECD TG 301 or 310 (Article 13(3) of REACH). Therefore, for a study according to OECD TG 301D, the following requirements must be met:

44 Reporting of the methodology and results

a) the source of the inoculum, its concentration in the test and any pre-conditioning treatment are reported (for OECD TG 301D, the concentration of the inoculum is set to reach a bacterial cell density of 10^4 to 10^6 cells/L in the test vessel).

b) the test design is reported (including the number of replicates).

c) the test conditions are reported (including the composition of the test medium, test temperature).

d) the results of measurements at each sampling point in each replicate is reported in a tabular form.

e) the calculation of the ThOD is described and justified.

45 In study (i) described as a ready biodegradability study:

46 Reporting of the methodology and results

a)-e) You have not provided any of the information listed above.

47 Based on the above, the reporting of the study is not sufficient to fully assess its reliability. More specifically, key aspects of the test design (number of replicates) and test conditions (inoculum origin, pre-treatment and density at the start of the test; test medium composition; test temperature) cannot be assessed. Therefore, it is not possible to independently assess whether the test was conducted under conditions that are consistent with the test guideline requirements. Furthermore, in the absence of reporting measured data, it is not possible to verify whether the validity criteria of the test guideline were met and whether the interpretation of the results is adequate.

48 Therefore, the requirements of OECD TG 301 D are not met.

3.2.1.2. The study (ii) does not qualify for a ready biodegradability test

49 To fulfil the information requirement, a study must comply with the OECD TG 301 or 310 (Article 13(3) of REACH). According to the Guidance on IRs and CSA, Section R.7. 9.5.1., "the optimum conditions in inherent biodegradability tests stimulate adaptation of the microorganisms thus increasing the biodegradation potential, compared to natural environments. Therefore, positive results in these tests should not be interpreted as evidence for rapid degradation in the environment".

50 The study (ii) is an inherent biodegradability study conducted according to EU Method C.9. (Zahn-Wellens Test).

51 Based on above, the study (ii) does not qualify for a ready biodegradability study and this information is rejected.

3.2.2. Assessment of your read-across adaptation (studies (iii) to (v))

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. In addition, ECHA identified endpoint-specific issue addressed below.

3.2.2.1. Inadequate or unreliable study on the source substances

53 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the study that must normally be performed for a particular information requirement, in this case the OECD TG 301C. Therefore, the following specifications must be met:

54 Reporting of the methodology and results

a) the source of the inoculum, its concentration in the test and any pre-conditioning treatment are reported (for OECD TG 301B, the concentration of the inoculum is set to reach a bacterial cell density of 107 to 108 cells/L in the test vessel. The suspended solid concentration is ≤ 30 mg/L).
b) the determination of the biodegradation using a specific chemical analytical method is reported.
c) the test design is reported (including the number of replicates).
d) the test conditions are reported (including the composition of the test medium).

e) the results of measurements at each sampling point in each replicate is reported in a tabular form.

f) the calculation of the ThOD is described and justified.

55 In study (iii) described as a ready biodegradability study according to OECD TG 301C:

56 Reporting of the methodology and results

a)-f) You have not provided any of the information listed.

57 On studies (iv) and (v) provided in your comments to the draft decision:

- for study (iv), you provide only the % degradation of the source substance after 28 day (*i.e.*, 97.34%).
- for the study (v), you provide a short summary of the study, containing limited data on the test design and the results (85.2% after 14 days).

58 As the reporting of these studies provided in your comment to the draft decision is not sufficient to conduct an independent assessment of their reliability, no conclusion on the compliance can currently be made.

59 Based on the above, the reporting of the studies (iii.) to (v) is not sufficient to fully assess their reliability. More specifically, key aspects of the test design (number of replicates) and test conditions (inoculum origin, pre-treatment and density at the start of the test; test medium composition) cannot be assessed. Therefore, it is not possible to independently assess whether the test was conducted under conditions that are consistent with the test guideline requirements. Furthermore, in the absence of reporting measured data, it is not possible to verify whether the validity criteria of the test guideline were met and whether the interpretation of the results is adequate.

60 Therefore, the studies submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameters of the corresponding OECD TG.

3.2.3. (Q)SAR results only are not sufficient to fulfil the information requirement under Annex VII, Section 9.2.1.1.

61 The Guidance on IRs and CSA, Section R.7.9.5.1. specifies that (Q)SARs for predicting ready biodegradation are not yet sufficiently accurate to predict rapid degradation. However, when no useful information on degradability is available (either experimentally derived or estimated), (Q)SAR predictions can be used as supporting evidence of that the substance is not rapidly degradable.

62 In your comments on the draft decision you provide information derived from QSARs (see (vi) and (vii) in Section 3.1. However for the reasons explained under Section 3.2.1. and 3.2.2., you dossier or your comments on the draft decision does not include any other reliable information on degradation.

63 As explained above, (Q)SARs predictions alone is not adequate to conclude on the persistence of the Substance. Therefore, this information does not fulfil the information requirement and your adaptation is rejected.

64 On the basis of the above, the information requirement is not fulfilled.

Reasons related to the information under Annex VIII of REACH

4. Screening for reproductive/developmental toxicity

65 A screening for reproductive/developmental toxicity (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1. This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Annex VIII, Section 8.7.1., Column 2 or a general adaptation rule under Annex XI.

4.1. Information provided

66 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) a prediction from DART (Developmental and Reproductive Toxicity) profiler and Cramer class determination extracted from the QSAR Toolbox (2020)

67 In addition, 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:

(ii) a carcinogenicity study in F344/N rats and B6C3F1 mice (1984) with the source substance phthalic anhydride (EC no. 201-607-5)

(iii) a carcinogenicity study phthalic acid esters and related compounds: structure-activity relationships (1986) with the source substance phthalic anhydride (EC no. 201-607-5)

(iv) Bioassay of phthalic anhydride for possible carcinogenicity (1979) with the source substance phthalic anhydride (EC no. 201-607-5)

4.2. Assessment of the information provided

4.2.1. (Q)SAR adaptation rejected

4.2.1.1. Inappropriate measures of robustness of the model

68 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.

69 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.

70 ECHA notes that Toolbox profilers are models developed for the purpose of identifying analogues and not to make predictions (as indicated on the official QSAR Toolbox website https://qsartoolbox.org/features/profiling/). In absence of measures of internal performance and predictivity, a profiler is not considered a scientifically valid approach to meet this information requirement.

71 Based on the above, your adaptation is rejected.

4.2.2. Read-across adaptation rejected

72 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 issue addressed below.

4.2.2.1. Inadequate or unreliable studies on the source substance

73 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 421 or 422. Therefore, the following specifications must be met:

f) at least three dose levels with concurrent controls are tested unless the study is conducted at the limit dose.

g) parameters for sexual function and fertility such as those for mating and fertility, duration of gestation, parturition and lactation are reported.

h) oestrous cycles are monitored.

i) offspring parameters such as number and sex of pups, stillbirths and live births, gross abnormalities, pup body weight, litter weight, anogenital distance, nipple retention in male pups are reported.

74 In studies (ii-iv) :

a) only two dose levels were tested.

b) data on parameters for sexual function and fertility such as those for mating and fertility, duration of gestation, parturition and lactation are missing.

c) data on oestrous cycles is missing.

d) data on number and sex of pups, stillbirths and live births, gross abnormalities, pup body weight, litter weight, anogenital distance, nipple retention in male pups are missing.

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

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

4.3. Justification for an adaptation of the screening study

77 You have submitted a testing proposal for an Extended one-generation reproductive toxicity (EOGRT) study addressed in a parallel decision. According to Annex VIII, Section 8.7.1., Column 2 and to prevent unnecessary animal testing, it is therefore not necessary for you to perform a screening study for reproductive/developmental toxicity if you provide a reliable EOGRT study.

78 Therefore, to comply with the information requirement under Annex VIII, Section 8.7.1., you are requested to provide a justification for an adaptation under Annex VIII, Section 8.7.1., Column 2.

5. Short-term toxicity testing on fish

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

5.1. Information provided

80 You have adapted the following standard information requirements by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2. In support of your adaptation, you have provided following information:

(i) a non-guideline short-term toxicity study on fish (1998) with the Substance.

(ii) a non-guideline short-term toxicity study on fish (1986) with the Substance.

(iii) a non-guideline short-term toxicity study on fish (1973) with the Substance.

(iv) a short-term (7 days) range-finding study for a long-term toxicity study on fish (1990) with the analogue Phthalic anhydride (EC No. 201-607-5).

81 In addition, in the comment to the draft decision, you provide the following additional studies with analogue substances as a part of your weight of evidence adapation:

(v) an short-term toxicity study on fish (1992) according to the OECD TG 203 with phthalic anhydride (EC no. 201-607-9);

(vi) an short-term toxicity study on fish (2007) according to the OECD TG 203 with hydrogen potassium phthalate (EC no. 212-889-4).

5.2. Assessment of the information provided on the Substance

5.2.1. Weight of evidence adaptation rejected

82 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.

83 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.

84 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.

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

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

87 In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation. Your weight of evidence approach has deficiencies that are common to all

information requirements under consideration and also deficiencies that are specific for these information requirements individually.

5.2.1.1. Relevance of the sources of information

88 Relevant information that can be used to support weight of evidence adaptation for the information requirement of Annex VIII, Section 9.1.3. includes similar information that is produced by the OECD TG 203 or other methods investigating short-term toxicity to fish.

89 All-provided sources of information in your dossier (studies (i) to (iv)) and in your comments on the draft decision (studies (v) and (vi)) may provide relevant information on the short-term toxicity to fish.

90 However, the reliability of these sources of information is significantly affected by the following deficiency:

5.2.1.2. Reliability of the sources of information

5.2.1.2.1. Read-across adaptation rejected (source of information (iv)-(vi))

91 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 issues with the reliability of the source studies as addressed below under Section 5.2.1.2.2.

5.2.1.2.2. The reliability of the sources of information (i) to (vi) cannot be assessed

92 To inform on short-term toxicity to fish, a study must normally comply with OECD TG 203 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the test duration is 96 hours or longer.
b) the analytical measurement of test concentrations is conducted.
c) the test design is reported (test organism, size and age are specified).
d) the test procedure is reported (fish loading).

93 For sources of information (i), (ii) and (iii):

a) in the studies (i) to (iii), the test duration was 48 hours;
b) for the sources of information (i) to (vi), you either do not specify whether analytical monitoring of exposure was performed or you do not provide the measured concentrations;
c) and d) for sources of information (v),you do not provide information on the test organism (species, age and size, fish loading) and the test procedure (fish loading). For source of information (vi), You do not provide information on the age and size of the test organsms.

~~94~~ Based on the above, sources of information (i) to (iii) provided in support of your adaptation have an exposure duration that is significantly shorter than the exposure duration specified in the test method normally required to meet this information requirement. Shorter exposure duration may have significantly affected the sensitivity of the reported studies. Furthermore, no information is available to demonstrate that test animals were satisfactorily exposed to the test material in any of the sources of information provided. Finally key information on the test design and procedure is missing for studies (v) and (vi) which further question their validity.

5.2.1.3. Conclusion

95 All sources of information (i) to (iv) in your dossier and additional sources of information (v) and (vi) in your comment to the draft decision provide information on mortality to fish. However, the reliability of this information is significantly affected by the deficiency listed above.

96 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for short-term toxicity to fish. As a result, your adaptation is rejected and the information requirement is not fulfilled.

97 In your comments on the draft decision, you also explain that, instead of performing a new OECD TG 203 study as requested, you propose to adapt the information requirement by using Annex VIII, section 9.1.3., column 2.

98 Should you decide to pursue your intended adaptation, ECHA bring your attention to the following observations. REACH Annex VIII, section 9.1.3., column 2 specifies that the short-term toxicity study does not need to be conducted if a long-term aquatic toxicity study on fish is available. At present no long-term toxicity study on fish is provided in the IUCLID dossier, therefore no conclusion on the compliance can currently be made. In any case, you remain responsible for complying with this decision by the set deadline.

Reasons related to the information under Annex IX of REACH

6. Pre-natal developmental toxicity study in one species

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

6.1. *Information provided*

100 You have provided a pre-natal developmental toxicity study in rats (1997) with the Substance.

6.2. *Assessment of the information provided*

6.2.1. The provided study does not meet the specifications of the test guideline

101 To fulfil the information requirement, a study must comply with OECD TG 414 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) at least 20 female animals with implantation sites for each test and control group are included.

b) the exposure duration is at least from implantation until one day prior to scheduled caesarean section.

102 In the provided study described as a pre-natal developmental toxicity study:

a) Only 11 females were included in each test and control group.

In your comments on the Draft Decision, you mention that despite the reduction of the number of animals to half of the number requested in the guideline, any potential critical effects should have been evident following the high doses used. ECHA understands that you justify the low number of animals by the absence of critical effect following the high doses. However, because of the low number of animals, the study has a low statistical power. In addition, under the applicable test guideline, the number of animals cannot be adapted based on the doses used, even if the doses are higher than the limit dose.

b) the exposure duration was from day 7 through day 16 of pregnancy and the dams were sacrificed on day 20.

103 Therefore, the information provided does not cover the specifications required by the OECD TG 414 and the information requirement is not fulfilled.

104 In your comment on the draft decision, you indicate your intention to adapt the PNDT first species information requirement by modifying the study design of the Extended One-Generation Reproductive Study OECD TG 443 submitted in your testing proposal (TPE-D-2114601804-56-01/D) in addition to the PNDT currently available in the dossier. More specifically, you intend to select 20 pregnant females in order to evaluate maternal toxicity. In addition, you propose to evaluate the "*surplus pups*" (*i.e.*, "*all pups not selected for Cohort 1A and 1B*").

105 We take note of your intention. However, we stress that any adaptation must meet the conditions set out in the corresponding provisions either the specific rules for adaptation

from column 2 of Annex IX section 8.7.2 or the general rules specified in Annex XI. You remain responsible for complying with this decision by the set deadline.

6.3. *Specification of the study design*

106 You have submitted a testing proposal for an Pre-natal developmental toxicity study addressed in a parallel decision. In your testing proposal, you specify that you intend to conduct the study on rabbit. Therefore, to cover the information requirement on pre-natal developmental toxicity study in a first species, a PNDT study according to the test method OECD TG 414 must be performed in rat.

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

108 Therefore, the study must be conducted in rats with oral administration of the Substance.

7. Long-term toxicity testing on aquatic invertebrates

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

7.1. Information provided

110 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 long-term toxicity study on *daphnia magna* (1997) with the analogue Phthalic anhydride (EC no. 201-607-5)

7.2. Assessment of the information provided

7.2.1. Read-across adaptation rejected

111 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 issue addressed below.

7.2.2. Inadequate or unreliable study on the source substance

112 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the study that must normally be performed for a particular information requirement, in this case the OECD TG 211. Therefore, the following specifications must be met:

113 Reporting of the methodology and results

a) the test design is reported (e.g. semi-static or flow-through, number of replicates, number of parents per replicate).

In your comments on the draft decision, you provide the following additional information: Semistic, with renewal every 24 hours; number of replicates: 10 per dose, 1 parent per vessel (80 ml/verssel)

b) the test procedure is reported (e.g. loading in number of Daphnia per litre, test

medium composition, feeding rate).

In the comments to the draft decision, you provide the following additional information : Feeding rate 0.1-0.15 mC/daphnia, test medium pH: 5.5-7.9, Hardness: 73-80 ($CaCO_3$), test temperature: 19.1-20.9°C

c) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations are provided.

In the comments to the draft decision, you provide the following additional information: Analytical method: HPLC

d) the full record of the daily production of living offspring during the test by each parent animalis provided.

In the comments to the draft decision, you do not provide the missing information. You specify that the tabulated results with the day by day numbers is not available for the study (i). You explain that the results are expressed with statistical evaluation as:

- Parent Daphnia median lethal concentration (21d—LC50) 55 mg/l (95 % confidence interval; 44-76 mg/l Calculated by the Probit method).
- 50% reproductive inhibitory concentration (EC50) 42 mg/l (95% confidence interval; 38-49 mg/l Calculated by the Logit method).
- Maximum no-effect concentration (NOEC) 16 mg/L (Calculated by Dunnett's multiple comparison test method).
- Minimum Effect Concentration (LOEC) 25 mg/L (Calculated by Dunnett's multiple comparison test method)

e) the number of deaths among the parent animals (if any) and the day on which they occurred is reported.

114 In the comments to the draft decision, you also state that "Despite the lack of a few details, this test has been assessed and accepted by the Japanese authority and the results commonly accepted as valid worldwide".

115 ECHA takes not of the additional information provided which partially resolve the issues identified above. However, you still did not provide adequate information addressed for the points c) to e) above.

116 As a result, ECHA maintains that the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, it is not possible to verify that exposure to the test material was satisfactorily maintained and that the interpretation of the study results is adequate.

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

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

8. Long-term toxicity testing on fish

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

8.1. Information provided

120 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 long-term toxicity study on fish (1990) with the analogue Phthalic anhydride (EC no. 201-607-5)

8.2. Assessment of the information provided

8.2.1. Read-across adaptation rejected

121 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 issue addressed below.

8.2.2. Inadequate or unreliable studies on the source substance

122 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the study that must normally be performed for a particular information requirement, in this case the OECD TG 210. Therefore, the following specifications must be met:

123 Technical specifications impacting the sensitivity/reliability of the test

a) at least 80 eggs, divided equally between at least four replicate test chambers, are used per concentration.

124 Characterisation of exposure

b) analytical monitoring must be conducted.

125 Reporting of the methodology and results

c) the test procedure is reported (composition of the test medium, fish loading).
d) data on mortality at each stage (embryo, larval and juvenile) measured daily and cumulative mortality are reported.
e) days to hatch, numbers of larvae hatched each day, and end of hatching are reported.
f) the number of healthy fish at end of test is reported.
g) data for length (specify either standard or total) and weight of surviving animals at the end of the test are reported.
h) the incidence, description and number of morphological abnormalities, if any, are reported.

126 In study (i) described as a long-term toxicity study on fish:

127 Technical specifications impacting the sensitivity/reliability of the test

a) 60 eggs were used per concentration.

128 Characterisation of exposure

b) no analytical monitoring of exposure was conducted.

129 Reporting of the methodology and results

c)-h) you have not provided any of this information.

130 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically:
  - the number of eggs used are fewer than that specified in the OECD TG 210. Consequently, the statistical power of study is too low.
  - you have not demonstrated that exposure to the test material has been satisfactorily maintained throughout the test.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically,
- it is not possible to verify that the test was conducted under conditions that are consistent with the test guideline requirement, that validity criteria were met and that the interpretation of the study results is adequate.

131 Therefore, this study does not provide a reliable coverage of the key parameters addressed in the OECD TG 210.

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

8.3. Study design and test specifications

133 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.).

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 deadline of the decision is set based on standard practices 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 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 07 December 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 requests or the deadline.

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 editorial change was made to request 4 to remove the obsolete alternative.

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]

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

1.1. Test methods, GLP requirements and reporting

(1) Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

(2) Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[2].

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

1.2. Test material

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

(1) Selection of the Test material(s)
The Test Material used to generate the new data must be selected taking into account the following:
- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

(2) Information on the Test Material needed in the updated dossier
- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- 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