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Helsinki, 04 May 2023

Addressees
Registrants of Purified Isophthalic Acid-PMC as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
18/09/2020

Registered substance subject to this decision ("the Substance")
Substance name: Isophthalic acid x
EC/List number: 204-506-4

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 ***9 February 2027***.

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

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

1. 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 IX of REACH

2. 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)

3. 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

4. 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)

5. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route, 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.

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

0.1.1. Read-across adaptation rejected

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

- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

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).

0.1.2. Predictions for 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(s):

TPA	terephthalic acid, EC No. 202-830-0.
DEHT/DOTP	bis(2-ethylhexyl) terephthalate, EC No. 229-176-9.

7 Regarding TPA, you provide the following reasoning for the prediction of toxicological properties: ”Isophthalic acid (benzene-1,3-dicarboxylic acid, the Substance) and terephthalic acid (benzene-1,4-dicarboxylic acid, the source substance) are structurally very similar, differing only in the positioning of the carboxylic acid groups. IPA does not contain any additional structural groups compared to TPA. This slight structural difference is unlikely to affect the basic toxicological properties of the substances”.

8 For DEHT you state in the read-across justification document, under the toxicological data, the following reasoning for the prediction of toxicological properties: “Data for DEHT show rapid absorption from the gastrointestinal tract and metabolism to liberate TPA and 2-ethylhexanol.”

9 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 substances.

10 We have identified the following issue with the prediction of toxicological properties:

0.1.2.1. *Inadequate read-across hypothesis for TPA and DEHT*

11 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must include an explanation why the properties of the Substance may be predicted from other substances in the group, i.e. a read-across hypothesis. This hypothesis should be based on recognition of the structural similarities and differences between the substances (Guidance on IRs and CSA, Section R.6.).It should explain why the differences in the chemical structures should not influence the toxicological properties or should do so in a regular pattern, taking into account that variations in chemical structure can affect both toxicokinetics (uptake and bioavailability) and toxicodynamics (e.g. interactions with receptors and enzymes) of substances (Guidance on IRs and CSA, Section R.6.2.1.3).

12 Your read-across hypothesis is only based on structural similarities and similarities in the physico-chemical properties of the source substances. You consider that these elements are a sufficient basis for predicting the toxicological properties of the Substance.

13 You have not substantiated how structural and physico-chemical similarity alone would explain similarity in the predicted endpoints and thus be sufficient to justify the toxicological predictions.

14 Physico-chemical similarity alone does not necessarily lead to predictable or similar toxicological properties. You have not provided a well-founded hypothesis to establish a reliable prediction for a toxicological property, explaining why the structural differences do not influence toxicokinetics and toxicodynamics of the substances, and thus why the properties of the Substance may be predicted from information on the source substances.

0.1.2.2. *Missing supporting information to compare the properties of the Substances and the sources substance TPA and DEHT*

15 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance(s) (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).

16 For the read-across from TPA, supporting information must include bridging studies to compare and to confirm your claim that both the source substance and the Substance have similar properties.

17 For thee read-across from DEHT, ECHA understands that this analogue substance would be biotransformed to TPA and 2-ethylhexanol and that you consider the similarity between TPA and IPA as the basis for the read-across. Therefore, supporting information must include toxicokinetic information on the formation of the similar compound (i.e. TPA), bridging studies to compare properties of the Substance and the source substance and information to confirm that the exposure to the non-common compound will not impact the prediction.

18 In the absence of such information, you have not established that a reliable prediction of the property under consideration of the Substance can be derived on the basis of your read-across hypothesis. Therefore, you have not provided sufficient supporting information to scientifically justify for the read-across.

0.1.2.3. *Inadequate or unreliable studies on the source substance*

19 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.

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20 Specific reasons why the studies on the source substance do not meet these criteria are explained further below under the applicable information requirements (See Request 2). Therefore, no reliable predictions can be made for these information requirements.

0.1.3. Conclusion on the read-across approach

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

Reasons related to the information under Annex VII of REACH

1. Ready biodegradability

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

1.1. Information provided

23 You have provided:

(i) a ready biodegradation study, OECD TG 301C (1976) with the Substance.
(ii) a ready biodegradation study, OECD TG 301B (1991) with the Substance.

1.2. Assessment of information provided

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

24 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 301, the following requirements must be met:

25 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 10^7 to 10^8 cells/L in the test vessel. The suspended solid concentration is ≤ 30 mg/L.
   - For OECD TG 301C, the concentration of the inoculum is set to reach a bacterial cell density of 10^7 to 10^8 cells/L in the test vessel.

b) The test temperature is reported.

c) For an OECD TG 301C, the determination of the biodegradation using a specific chemical analytical method is reported.

26 In studies (i) and (ii) described as studies on ready biodegradability:

27 Reporting of the methodology and results

- For study (i), you have not provided any information listed a)-c) above.
- For study (ii), you have not provided any information listed a)-b) above.

28 Based on the above, the reporting of the studies is not sufficient to conduct an independent assessment of their reliability. More specifically, key aspects of the test conditions (inoculum origin, pre-treatment and density at the start of the test; test 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.

29 Therefore, the requirements of OECD TG 301 B/C are not met and the information requirement is not fulfilled.

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

Reasons related to the information under Annex IX of REACH

2. Pre-natal developmental toxicity study in one species

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

2.1. Information provided

32 You have provided:

(i) a developmental toxicity study similar to OECD TG 414 (1991) with the Substance
(ii) a sexual differentiation study, no TG followed (2000) with the source substance DEHT

33 You have also adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on the following experimental data:

(iii) a developmental toxicity study similar to OECD TG 414 (1990) with the source substance TPA
(iv) a developmental toxicity study according to OECD TG 414 (2005) with the source substance DEHT
(v) a developmental toxicity study according to OECD TG 414 (2001) with the source substance DEHT

2.2. Assessment of the information provided

2.2.1. The provided study (i) does not meet the specifications of the test guideline(s)

34 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:

b) the highest dose level aims to induce toxicity or aims to reach the limit dose;
c) the test chemical is administered via oral gavage; Justification should be provided for other routes.

35 In study (i) described as a pre-natal developmental toxicity study:

a) the highest dose levels tested was 9.07 mg/m³, which is below the limit dose of the test guideline, and no adverse effect were observed, and no justification is provided for the dose setting;
b) the substance was administered by inhalation without justification.

36 The study (i) does not cover the specification(s) required by the OECD TG 414.

2.2.2. Study (ii) not adequate for the information requirement

37 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 are included for each test and control group to ensure a statistical power equivalent to OECD TG 414;
b) the foetuses are examined for external, skeletal and soft tissue alterations (variations and malformations), number of resorptions and/or live foetuses.

38 The study (ii) is described as a sexual differentiation study in male rats. This study has not been conducted under a specific test guideline and does not cover the key parameters of OECD TG 414. In addition, the study shows the following:

a) only 8 female animals (i.e., less than 20 female animals) with implementation sites are included in each group, and therefore the statistical power is not equivalent to OECD TG 414;
b) the foetuses are not examined for external, skeletal and soft tissue alterations (variations and malformations), number of resorptions and/or live foetuses are not investigated.

39 Therefore, study (ii) is not adequate for the information requirement and is therefore rejected.

2.2.3. Weight of evidence assessment (studies (iii), (iv) and (v)

40 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.

41 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.

42 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.

43 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.

44 You have not included a justification for your weight of evidence adaptation, 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.

45 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.

46 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.7.2 at Annex IX includes similar information that is produced by the OECD TG 414 on one species. The following aspects are covered: 1) prenatal developmental toxicity, 2) maternal toxicity, and 3) maintenance of pregnancy.

47 Developmental toxicity includes information after prenatal exposure on embryonic/foetal survivial(number of live foetuses; number of resorptions and dead foetuses, postimplantation loss), growth (body weights and size) and structural malformations and variations (external, visceral and skeletal).

48 Maternal toxicity includes information after gestational exposure on maternal survival, body weight and clinical signs.

49 Maintenance of pregnancy includes information on abortions or early delivery as a consequence of gestational exposure.

50 The sources of information (iii), (iv) and (v) provide relevant information on developmental toxicity, maternal toxicity and maintenance of pregnancy. However, the reliability of the sources of information (iii), (iv) and (v) is significantly affected by the deficiencies identified and explained under Appendix on Reasons common to several requests, and cannot contribute to the conclusion on this key element.

51 Information from source substance(s) can be used as part of weight of evidence adaptation if the read-across is accepted.

52 The information from (iii), (iv) and (v) with a read across source substance is already rejected under Appendix 0.1. Therefore it cannot be used as part of the weight of evidence adaptation.

53 Therefore, no conclusion can be drawn on prenatal developmental toxicity as required by the information requirement.

54 In addition, according to ECHA Guidance[4] the highest dose level should be intended to produce some toxicity (or to reach the oral limit dose of 1000 mg/kg bw/day) to provide adequate information on reproductive toxicity for the purpose of both classification (including categorisation within the Reproductive toxicity hazard class) and risk assessment. Dose level selection (and vehicle used) must be justified and documented to allow independent evaluation of the choice made.

55 The highest dose level in the sources of information (iii) did not induce any toxicity and you have not shown that the aim was to induce toxicity. Therefore, the dose level selection was too low, and the studies do not fulfil the criterion set in OECD TG 414.

56 Finally, considering the route of exposure in the source of information (iii), OECD TG 414 states that "*The test chemical or vehicle is usually administered orally by intubation. If another route of administration is used, the tester should provide justification and reasoning for its selection*". You have not provided any justification why the inhalation route was chosen.

57 Taken together, the relevant information on prenatal developmental toxicity provided is not reliable.

58 Your weight of evidence adaptation does not include any relevant and reliable sources of information to conclude on the property of prenatal developmental toxicity on one species. Therefore your adaptation is rejected and information requirement is not fulfilled.

59 Therefore, the information requirement is not fulfilled.

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

2.3. Specification of the study design

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

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

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

3. Long-term toxicity testing on fish

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

3.1. Information provided

65 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided following information:

66 The study does not need to be conducted as:

- All the identified uses of the substance are assessed as safe for the environment.
- The Substance will not be directly applied to water.
- Exposure to aquatic system is not expected to occur.
- The Substance is not released from articles manufactured from polyesters following polymerisation.
- The Substance is readily biodegradable.

3.2. Assessment of the information provided

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

67 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).

68 Your adaptation is therefore rejected.

69 Therefore, the information requirement is not fulfilled.

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

Reasons related to the information under Annex X of REACH

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

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

4.1. Information provided

72 You have not submitted any information for this requirement.

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

4.2. Specification of the study design

74 A PNDT study according to the test method OECD TG 414 should be performed in rabbit or rat as preferred second species, depending on the species tested in the first PNDT study (request 2 in this decision).

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

76 Based on the above, the study must be conducted in rabbit or rat with oral administration of the Substance.

5. Extended one-generation reproductive toxicity study

77 An extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is an information requirement under Annex X, Section 8.7.3. Furthermore column 2 defines the conditions under which the study design needs to be expanded.

78 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 two generation study (2003) with the source substance TPA

5.1.1. Read-across adaptation rejected

79 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.

80 Based on the above, the study is not an adequate basis for your read-across predictions.

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

5.2. Specification of the study design

5.2.1. Species and route selection

82 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.).

5.2.2. Pre-mating exposure duration

83 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.

84 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.).

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

5.2.3. Dose-level setting

86 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, paragraph 22; OECD GD 151, paragraph 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.

87 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, paragraph 18) in the P0 animals.

88 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.

89 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) 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.

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

91 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.

5.2.4. Cohorts 1A and 1B

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

5.2.4.1. *Histopathological investigations in Cohorts 1A and 1B*

93 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, paragraph 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.

5.2.4.2. *Splenic lymphocyte subpopulation analysis*

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

5.2.4.3. *Investigations of sexual maturation*

95 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, paragraph 12 in conjunction with OECD TG 443, paragraph 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.

5.2.4.4. *Further expansion of the study design*

96 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 Annex IX/X, Section 8.7.3., Column 2. 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).
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

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 14 March 2022.

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.

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

In your comments you agreed to the draft decision. ECHA took your comments into account 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.

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]
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[redacted]	[redacted]	[redacted]
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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].

(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