~~Confidential~~

Helsinki, 09 November 2023

Addressees
Registrants of JS_Lanthanum oxide as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
11/12/2019

Registered substance subject to this decision ("the Substance")
Substance name: Lanthanum oxide
EC/List number: 215-200-5

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***14 June 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. Water solubility (Annex VII, Section 7.7.; test method: OECD GD 29)

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

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

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

4. Long-term toxicity testing on fish also requested below (triggered by Annex VIII, Section 9.1.3., column 2) only if the results of Request 1 show the Substance is poorly water soluble (i.e. water solubility < 1 mg/L)

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

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

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

Information required depends on your tonnage band

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

In the requests above, the same study has been requested under different Annexes. This is because some information requirements may be triggered at lower tonnage band(s). In such cases, only the reasons why the information requirement is triggered are provided

for the lower tonnage band(s). For the highest tonnage band, the reasons why the standard information requirement is not met and the specification of the study design are provided. Only one study is to be conducted; all registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the others under Article 53 of REACH.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

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

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

Appeal

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

Failure to comply

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

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

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

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

Appendix 1: Reasons for the decision

Contents

0. Reasons common to several requests

0.1. Assessment of 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:

- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Long-term toxicity testing on fish (Annex VIII, Section 9.1.3, column 2)

2 ECHA has considered the scientific and regulatory validity of your read-across approaches 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 toxicological properties

5 You provide a justification for your read-across in CSR, Part B, Sections 1.4 and 5.9.3.

6 You predict the properties of the Substance from information obtained from the following source substance: "*Mixed metal oxides including lanthanum oxide*".

7 You provide the following reasoning for the prediction of toxicological properties: "Studies with […] mixtures of oxides and lanthanum carbonate which has a comparable solubility to lanthanum oxide and is regarded to be very similar with regard to its toxicokinetics are considered relevant for read across to lanthanum oxide".

8 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

9 We have identified the following issues with the predictions of toxicological properties:

0.1.1.1. Missing supporting information

10 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.).

11 Supporting information must include bridging studies to compare properties of the Substance and source substances, and information on the impact of exposure parent compounds on the prediction.

12 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

13 Furthermore, exposure to the Substance and of the source substance(s) may also lead to exposure to other compounds than the common compound of interest. The impact of exposure to these non-common compounds on the prediction of properties of the target needs to be assessed to ensure that a reliable prediction can be made.

14 You have provided the robust study summary for a three-generation reproductive toxicity study (1975) with the source substance "*Mixed metal oxides including lanthanum oxide*", but you have not provided any bridging studies of comparable design and duration that allow comparison between the properties of the Substance and the source substance "*Mixed metal oxides including lanthanum oxide*".

15 You identify the test substance as "*Mixed metal oxides including lanthanum oxide*", to which test animals were exposed via the diet. In the robust study summary, you state that the following "metal oxides" make up the test substance: [redacted]. You have provided a table describing the concentrations at which these components of the test substance are present in the diet. You have not provided any justification or supporting information that addresses the potential impact of these non-common compounds on the outcome and predictability of the study.

16 In the absence of such supporting information, you have not established that the Substance and the source substance(s) are likely to have similar properties. Therefore, you have not provided sufficient supporting information to scientifically justify the read-across.

0.1.2. Predictions for ecotoxicological properties

17 You provide a read-across justification document in CSR, Part B, Section 1.4.

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

Source substance 1	Lanthanum chloride, hydrate, EC No. 640-503-8.
Source substance 2	Lanthanum chloride, anhydrous , EC No. 233-237-5.
Source substance 3	Cerium dioxide, EC No. 215-150-4.

19 You provide the following reasoning for the prediction of for the prediction of ecotoxicological and environmental fate properties: "*It is reasonably assumed that the La^{3+} cation will be the relevant species for the toxicity and ecotoxicity of lanthanum oxide*" and that "[..] *Ce^{3+} ion has the same oxidation state and the same ionic radius as La^{3+}*" .

20 ECHA understands that your read-across hypothesis is based on the production of common or similar soluble ionic metal species. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

21 We have identified the following issues with the predictions of aquatic toxicity:

0.1.2.1. Inadequate read-across hypothesis for the read-across from Cerium dioxide

22 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.

23 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 also explain why the differences in the chemical structures should not influence the ecotoxicological 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).

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

25 You have not substantiated how physico-chemical similarity between lanthanum oxide and cerium oxide alone would explain similarity in the predicted property and thus be sufficient to justify the ecotoxicological predictions.

26 Physico-chemical similarity alone does not necessarily lead to predictable or similar ecotoxicological properties. You have not provided a well-founded hypothesis to establish a reliable prediction for an ecotoxicological 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

27 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.).

28 Supporting information must include transformation/dissolution information on the formation of the common ionic metal species and bridging studies to compare properties of the Substance and source substances.

29 As indicated above, your read-across hypothesis is based on the production of common or similar ionic metal species from the Substance and the source substances. In this context, information characterising the rate and extent of the transformation/dissolution of the Substance and of the source substances is necessary to confirm the production of the proposed ionic metal species and to assess the potential exposure to the parent compounds.

30 Furthermore, also indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substances is necessary to confirm that both substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substances.

31 However, you have not provided any experimental information on the transformation/dissolution of the Substance nor the source substances to support your claims regarding formation of a common or similar compounds.

32 Furthermore, for the source substances, you provide the studies used for the predictions in the registration dossier. Apart from these studies, your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data for the Substance that would confirm that the target and source substances cause the same type of effects.

33 In the absence of this information, you have not provided supporting evidence establishing the extent that the proposed common or similar soluble ionic metal species is formed as assumed in your read-across hypothesis. Furthermore, for the read-across from Cerium oxide, you have not established that the Substance and the source substance are likely to have similar properties. Therefore, you have not provided sufficient supporting information to scientifically justify your read-across hypothesis.

0.1.2.3. Adequacy and reliability of source studies

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

(1) be adequate for the purpose of classification and labelling and/or risk assessment;
(2) have adequate and reliable coverage of the key parameters addressed in the corresponding study that shall normally be performed for a particular information requirement;
(3) cover an exposure duration comparable to or longer than the corresponding study that shall normally be performed for a particular information requirement if exposure duration is a relevant parameter.

35 Specific reasons why the studies on the source substances do not meet these criteria are explained further below under the applicable information requirement sections 2. Therefore, no reliable predictions can be made for these information requirements.

0.1.3. Conclusion on the read-across approach

36 For the reasons above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s).

37 In your comments to the draft decision you specify that an updated read-across justification for your approach will be provided in an upcoming dossier update. However, as the read-across justification information is not currently available in your registration dossier, no conclusion on the compliance can currently be made.

38 Your read-across approach under Annex XI, Section 1.5. is rejected.

0.2. Assessment of weight of evidence adaptations

39 You have adapted the following standard information requirements by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2:

- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

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 for each of the relevant information requirement, 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, common to all information requirements under consideration, ECHA has nevertheless assessed the validity of your adaptation.

46 The common deficiency is set out here, while the specific ones are set out under the information requirement concerned in the Sections below.

0.2.1. Reliability of the read across approach

47 Section 0.1 of the present Appendix identifies deficiencies of the read across approach used in your dossier. These findings apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptations.

Reasons related to the information under Annex VII of REACH

1. Water solubility

48 Water solubility is an information requirement under Annex VII to REACH (Section 7.7). However, information on transformation/dissolution in aqueous media shall be provided when the substance is a metal or sparingly soluble metal compound (Section 7.7., Column 2).

1.1. Triggering of the information required

49 Based on a water solubility experiment according to the key OECD TG 105 submitted in your dossier, the Substance is concluded to be a sparingly soluble metal compound as its solubility in water was determined to be 69.6 µg/L at 20°C.

50 Therefore, water solubility is required in accordance with Section 7.7., Column 2.

1.2. Information provided

51 Guidance on IRs and CSA, Section R.7.1.7.3. specifies that, for metal or sparingly soluble metal compound, water solubility must be determined according to the OECD GD 29 (Transformation/Dissolution of metals and metal compounds in aqueous media).

52 However, you have provided OECD TG 105 studies (2007) and a water solubility estimate from a secondary source with no description of the test method but no information on the transformation/dissolution in aqueous media of the Substance.

53 In the absence of information on transformation/dissolution in aqueous media, the information requirement set out in Section 7.7., Column 2 is not fulfilled.

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

1.3. Study design and test specifications

55 Under Section 4.5. of your technical dossier a key study on granulometry according to Guidance document, ECB/TM (1996) and the Draft guidance document, EUR 20268 EN (2002), Part 5.2 (Laser scattering / diffract) shows that the registered substance have particle size ranging between 0.3 µm and 300 µm with a mass median diameter (D_{50}) of 23.8±2 µm. For powders (particle size < 1mm), the test must be conducted using a test material having the smallest representative particle size on the market. OECD TG GD 29 on Transformation/Dissolution of metals and metal compounds in aqueous media specifies that the specific surface area of the test material must be determined.

2. Growth inhibition study aquatic plants

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

2.1. Information provided

57 You have adapted this information requirement by using weight of evidence based on the following experimental data:

i. an OECD TG 201 study (1995) with the analogue substance Lanthanum chloride, hydrate (EC 640-503-8)
ii. an OECD TG 201 study (2007) with the analogue substance Cerium dioxide (EC 215-150-4)
iii. a non guideline study (2002) on duckweed (Lemna minor L.) with the analogue substance Lanthanum chloride, anhydrous (EC 233-237-5)

58 ECHA understands that your weight of evidence approach relies on grouping and read-across approach under Annex XI, Section 1.5.

2.2. Assessment of the information provided

59 As explained in Section 0.2, it would be sufficient to reject your weight of evidence adaptation based on the fact that you have not submitted any justification for your adaptation.

60 In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation. Your weight of evidence approach has also deficiencies that are specific for this information requirement and they are set out in the Sections below.

61 Relevant information that can be used to support weight of evidence adaptation for the information requirement of Annex VII, Section 9.1.2 includes similar information that is produced by the OECD TG 201 or the OECD 221. OECD TG 201 and OECD 221 requires the study to investigate the following key element:

- the concentrations of the test material leading to a 50 % and 0% (or 10%) inhibition of growth by the end of the exposure phase

62 The sources of information (i) to (iii) provide relevant information on the key element listed above. However, the reliability of these sources of information is significantly affected by the following deficiencies:

2.2.1. Read-across adaptation rejected for study (i) to (iii)

63 As explained in Section 0.1.2., 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.

64 In you comments on the draft decision, you state that "*a document, summarising and discussing all available data on the growth inhibition of rare earths to aquatic plants*" will be added to the dossier. On this basis ECHA undesrands that, you intend to use this as supporting information to your grouping and read-across approach according to Annex XI, Section 1.5, of the REACH Regulation. As the information in your comments is not sufficient for ECHA to make any assessment, no conclusion on the compliance can currently be made.

2.2.2. The provided study (i) does not meet the specifications of the applicable test guideline

65 A Growth inhibition study on aquatic plants must follow the specifications of the OECD TG 201 or the OECD TG 221 and the requirements of OECD GD 23 if the substance is difficult to test. Therefore, for a study conducted according to OECD TG 201, the following specifications must be met:

66 Reporting of the methodology and results

a) 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;

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

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

67 Your registration dossier provides an OECD TG 201 study (study i) showing the following:

68 Reporting of the methodology and results

a) you report that algal biomass was determined using a counting chamber initially and a spectrophotometer at 720 nm thereafter. However, you have not reported evidence of correlation between the measured parameter and dry weight or cell numbers over the range of biomass occurring in the test;

b) tabulated data on the algal biomass determined daily for each treatment group and control are not reported;

c) no information is provided on the analytical method. The results of the analytically determined exposure concentrations are not provided.

69 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, you have not provided adequate information on the method used to determine algal biomass, on the measured biomass data, and on the analytical verification of exposure concentrations. Therefore, it is not possible to verify whether the validity criteria of the OECD TG 201 were met and to verify the interpretation of the results of this study.

70 Therefore, this source of information does not follow some of the essential specifications of OECD TG 201 and its reliability cannot be currently assessed.

2.2.3. The provided study (iii) does not meet the specifications of the Guidance on IRs and CSA

71 To fulfil the information requirement, studies should be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the Agency as being appropriate (Article 13(3) of REACH). As specified in Guidance on IRs and CSA, Section R.7.8.4.1, for the evaluation of data from non-standard ecotoxicity tests on aquatic plants the following specifications must be met:

72 Key parameter to be measured

a) the concentrations of the test material leading to a 50 % and 0% (or 10%) inhibition of growth at the end of the test are estimated.

73 Characterisation of exposure

b) the preparation of test solutions must ensure exposure to the test material.

74 Reporting of the methodology and results

c) tabulated data on the biomass determined at appropriate frequency for each treatment group and control are not reported.

75 Your registration dossier provides a non-guideline study on Lemna sp. (study iii) showing the following:

76 Key parameter to be measured

a) you report an unbound value for NOEC (196h) ≥ 2.45µg/l based growth rate.

77 Characterisation of exposure

b) for the test solutions the study reports that the Lanthanum is mainly associated with EDTA. Specifically, it is reported that "*Speciation calculations showed all La to be in solution up to pH 5.6 (initial pH 5.05) and for more than 99.9% associated with EDTA*". Therefore, the presence of a chelating agent in the test medium led to reducing significantly the exposure to the test material.

Reporting of the methodology and results

c) no tabulated data on the biomass is provided.

78 Based on the above,

- the information provided does not cover the key parameter required by non-standard ecotoxicity tests on aquatic plants. While the value is reported as being based on growth rate, you do not define on which measurement the growth rate is calculated on (i.e. front measurement, total frond area, dry weight or fresh weight).
- there is a critical methodological deficiency resulting in the rejection of the study results. More specifically, as shown from the information on the test solution the exposure of the organism to the substance was minimal and thus no conclusion on possible effects can be drawn from the study.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, you have not provided adequate reporting of biomass measurement. Therefore, an independent assessment of the study is not possible.

79 Therefore, the source of information does not follow some of the essential specifications of the Guidance on IRs and CSA, Section R.7.8.4.1, for the evaluation of data from non-standard ecotoxicity tests on aquatic plants.

80 Based on the above, the studies (i) and (iii) do not provide an adequate and reliable coverage of the key parameter addressed by the OECD TG 201 or the OECD 221 or of similar test methods as specified in the Guidance on IRs and CSA, Section R.7.8.4.1. Furthermore, the read-across predictions are rejected for the reasons explained under Section 0.1.2. The deficiencies affecting the reliability of sources (i) to (iii) are so significant that these sources of information cannot contribute to the conclusion on the key parameter investigated by the study normally required.

2.2.4. Conclusion on the weight-of-evidence adaptation

81 In summary, the sources of information (i) to (iii) provide relevant information on the key elements of this information requirement. However, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for growth inhibition of aquatic plants (algae preferred).

82 As it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for growth inhibition of aquatic plants (algae preferred). Therefore, your adaptation is rejected and the information requirement is not fulfilled.

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

2.3. Study design and test specifications

84 The Substance is difficult to test due to its low water solubility. OECD TG 201 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 201. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

Reasons related to the information under Annex VIII of REACH

3. Short-term toxicity testing on fish

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

3.1. Information provided in your dossier

86 You have provided:

i. an OECD 203 study (2000) with the Substance

87 In addition, you have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data:

ii. an OECD 203 study (2000) with the analogue substance Cerium carbonate, EC 208-655-6

3.2. Assessment of the information provided in your dossier

3.2.1. The provided study on the Substance (study i) and the source substance (study ii) do not meet the information requirement

88 To fulfil the information requirement, a study must comply with the OECD TG 203 (Article 13(3) of REACH). Therefore, the following specifications must be met:

89 Validity criteria

a) the analytical measurement of test concentrations is conducted;

90 Technical specifications impacting the sensitivity/reliability of the test

b) the test is conducted on juveniles of similar age (or size);

91 Reporting of the methodology and results

c) mortalities and sub-lethal effects (*e.g.* with regard to equilibrium, appearance, ventilator and swimming behaviour) are reported. The frequency of observations includes at least 2 observations within the first 24 hours and at least two observations per day from day 2 to 4.

92 Your registration dossier provides OECD TG 203 studies (study i. and ii.) showing the following:

93 Validity criteria

a) no analytical measurement of test concentrations was conducted in studies i. and ii.;

94 Technical specifications impacting the sensitivity/reliability of the test

b) studies i. and ii. were conducted on Danio rerio with a test animal mean size of c.a. 3 cm (i.e., above the recommended size range of 1-2 cm as specified in Annex 2 of OECD TG 203)

95 Reporting of the methodology and results

c) tabulated data on mortalities and sub-lethal effects (*e.g.* with regard to equilibrium,

appearance, ventilator and swimming behaviour) obtained on at least 2 observations within the first 24 hours and at least two observations per day from day 2 to 4 for each treatment group and control are not reported for studies i. and ii.

96 Based on the above,

- the validity criteria of OECD TG 203 are not met for studies i. and ii.

  In your comments on the draft decision, regarding the study (i) you state that "*due to the very low solubility an analytical determination of the test substance was not possible*". However, you do not provide any further documentation and justification to support this statement.

- there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically the size of the test animals was above the recommended size range for the test species and therefore you have not demonstrated that the studies i. and ii. were conducted on juveniles.

  In your comments on the draft decision, regarding the study (i) you state that the "*slightly larger fish size than specified in the current guideline is unlikely to invalidate the study*". However, you do not provide any information on what extent the deviation of the fish size affected the sensitivity of the test.

- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, you have not provided adequate reporting of the results obtained in studies i. and ii.

  In your comments on the draft decision, regarding the study (i) you state that the "*reporting of the existing acute study can be made in more detail, although no toxicity was observed at any time point*". The information in your comments is not sufficient for ECHA to make an assessment.

97 In your comments on the draft decision regarding the study (i) you acknowledge the deficiencies identified above but the information in your comments does not address the deficiencies.

98 Therefore, the requirements of OECD TG 203 are not met for studies i. and ii.

3.2.2. Read-across adaptation rejected

99 As explained in Section 0.1.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

100 As stated in section 0.1 based on your comments to the draft decision ECHA understands that you do not intent to use Cerium carbonate in a read-across approach to fulfil the information requirements for the endpoints presented above.

3.3. Information provided in your comments on the draft decision

101 In the comments to the draft decision, you do not agree to perform the requested study. Instead, you indicate that you intend to adapt this information requirement by means of grouping and read-across according to Annex XI, Section 1.5, of the REACH Regulation. You specifically refer to "*an OECD 204 conducted with the soluble lanthanum trichloride*" and that "*reliable short term data are available for the water soluble La(NO3)3*".

ECHA take note of your intentions to submit a read-across approach for this information requirement. However, as the information in your comments for study (i) and the OECD

204 on lanthanum trichloride is not sufficient for ECHA to make an assessment, no conclusion on the compliance can currently be made.

102 Based on the above, the information requirement is not fulfilled, and you remain responsible for complying with this decision by the set deadline.

3.4. Study design and test specifications

103 OECD TG 203 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design and test specifications' under Request 2.

4. Long-term toxicity testing on fish

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

4.1. Triggering of the information requirement

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

106 For the reasons explained under Request 1, the information requirement on water solubility is not fulfilled.

107 If the results of the information requested under Request 1 show that the Substance is poorly water soluble (i.e. water solubility under relevant conditions < 1 mg/L), information on long-term toxicity on fish will need to be provided.

4.2. Information provided

108 As explained in Request 3, you have incompliant information on short-term toxicity to fish. Furthermore, you have adapted the information requirement for long-term toxicity on fish for the Substance using read-across.

4.3. Assessment of the information provided

109 The examination of the information provided, as well as the selection of the requested test and the test design are addressed under section 5.

Reasons related to the information under Annex IX of REACH

5. Long-term toxicity testing on fish

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

5.1. Information provided

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

i. an OECD 204 (1995) with the analogue substance Lanthanum chloride, hydrate (EC 640-503-8)

5.2. Assessment of the information provided

5.2.1. Read-across adaptation rejected

112 As explained in Section 0.1.2., 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(s) addressed below.

5.2.2. The OECD TG 204 is not a valid test guideline to meet this information requirement

113 To fulfil the information requirement, a study must be a long-term fish test. Guidance on IRs and CSA, Section R.7.8.4.1. specifies that only studies in which sensitive life-stages (juveniles, eggs and larvae) are exposed can be regarded as long-term fish tests.

114 Your registration dossier provides an OECD TG 204 study in which only adults were exposed to the test material.

115 This study does not provide information on the toxicity of the test material to relevant sensitive life-stages (i.e. juveniles, eggs and larvae). OECD TG 204 only provides information on prolonged acute toxicity and, based on the above, it does not qualify as a long-term fish test. Therefore, this information is rejected.

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

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

5.3. Study design and test specifications

118 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.).

119 OECD TG 210 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design and test specifications' under Request 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).

All Guidance on REACH is available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

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

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

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

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

Appendix 2: Procedure

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 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.

In your comments on the draft decision, you requested an extension of the deadline to provide information from 24 to 40-46 months from the date of adoption of the decision.

You justified the request by additional time required to complete the testing due to limited capacity of CROs. You provide documentary evidence from one CRO that cannot start any OECD TG 443 study before Q2 2023.

On this basis, ECHA has extended the deadline to 40 months.

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

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s) and referred the modified draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

In addition, you provided comments on the draft decision, i.e. comments which do not address the proposal for amendment(s). Therefore, these comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5).

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-81 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Following the Board of Appeal’s decision in cases A-002-2022 and A-003-2022, ECHA removed from this decision the information requirement for an Extended one-generation reproductive toxicity study (EOGRTS; Annexes IX or X, Section 8.7.3.). This information requirement may be addressed in a separate decision.

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

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

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[3].

[3] https://echa.europa.eu/manuals