~~Confidential~~

Helsinki, 09 November 2023

Addressees
Registrants of JS_Lanthanum trichloride 2 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
13/09/2013

Registered substance subject to this decision ("the Substance")
Substance name: Lanthanum chloride, anhydrous
EC/List number: 233-237-5

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 ***16 August 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. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: OECD TG 471, 2020)

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

4. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days) requested below (Annex VIII, Section 8.6.1.)

5. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats

6. 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

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

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

9. 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

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

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 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:

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- 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).

0.1.1. 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):

Source substance 1	Lanthanum nitrate hexahydrate ([redacted]%), CAS No. 6487-39-4.
Source substance 2	Lanthanum carbonate ([redacted]%), CAS No. 587-26-8.
Source substance 3	Lanthanum carbonate octahydrate ([redacted]%), CAS No. 6487-39-4
Source substance 4	Lanthanum oxide (purity not known), CAS No. 1312-81-8

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

- *"It is supposed that environmental and toxicological effects can be attributed mainly to the Lanthanum cation."*
- *"Lanthanum chloride is an inorganic salt of a weak base, which is highly water soluble and nearly completely dissociates in solution."*
- *"Lanthanum nitrate, its hydrate and Cerium chloride, are highly water soluble. Since these substances are also salts of weak bases, they dissociate in the same manner as Lanthanum chloride."*
- *"Even though Lanthanum carbonate, its hydrate and Lanthanum oxide are practically insoluble in water, they dissociate in the acidic environment of the upper gastrointestinal tract and free Lanthanum ions occur."*

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 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 toxicokinetic information on the formation of the common compound to compare properties of the Substance and source substances.

12 As indicated above, your read-across hypothesis is based on the (bio)transformation of the Substance and of the source substance(s) to a common compound(s), i.e. the target and the source substances dissociate in the upper gastrointestinal tract to release free Lanthanum ions. In this context, information characterising the rate and extent of the (bio)transformation/dissolution of the Substance and of the source substance(s) is necessary to confirm the formation of the proposed common (bio)transformation product and to assess the impact of the exposure to the parent compounds as well as to Lanthanum ion itself.

13 In you dossier, you have not provided any experimental information, about the (bio)transformation of the Substance nor the (source substance(s) to support your claims regarding formation of a similar common compound with a similar bioavailability.

14 In your comments on the draft decision, you provide the following arguments to support your hypothesis that all the lanthanum compounds dissociate in the upper gastrointestinal tract to release free lanthanum ions:

- The inorganic counterions (such as chloride or carbonate) are extremely widely studied and understood and "*the common precursor and / or likely common breakdown products of lanthanum chloride anhydrous will be common to all the Lanthanum Salts: the* La^{3+}";
- *"Lanthanum carbonate, Lanthanum hydrate and Lanthanum oxide will produce the same result because the dissolved substance will become* $La^{3+}(Cl^{-})_3$ *in the acidic environment of human stomach*";
- "*The biotransformation/dissolution information can be supplemented by the study of* [redacted] *2019 which reports that the relaxation times for Lanthanum chloride (5.4.4.), Lanthanum oxide (5.4.8) and Lanthanum carbonate (5.4.12) are all very similar in a pH range of 2-5*. […] *Therefore, since all three of the tested Lanthanum Salts behave in a similar manner when dissolved, their availability/dissolution profiles are sufficiently similar that they should be treated as a single group*";
- "*Toxicokinetic information is given in the FDA (*[redacted]*) and EMA (*[redacted]*) application for* [redacted]".

15 However, the main problem identified for the read-across between the soluble and insoluble substances, namely the lack of experimental data showing that a similar amount of lanthanum will become bioavailable after dissolution, still remains.

16 Although it is theoretically conceivable that, at the pH of the upper GI tract, complete hydrolysis and subsequent uptake of the La^{3+} ions may occur, you have not provided supporting (experimental) information that would prove this claim under physiologically relevant conditions. The kinetic rate of such reaction is valuable in improving the confidence in the read-across approach, even if obtained with simulated GI fluids.

17 You also make reference to a study by [redacted] (2019) without providing the study. The relaxation times referred to in this study seem to belong to an analytical chemistry investigation. This may support that under controlled conditions of a chemical lab, the source substance Lanthanum carbonate (completely) dissociates under acidic conditions. However, this information is of low relevance to the conditions and effects *in vivo*.

18 You refer to toxicokinetic information from the FDA ([redacted]) and EMA ([redacted]) application for [redacted]. However, none of these studies were provided in the dossier and in your comments and therefore an independent assessment is not possible.

19 In the absence of this information, you have not provided supporting evidence establishing that the proposed common (bio)transformation product is formed as assumed in your read-across hypothesis. Therefore, you have not provided sufficient supporting information to scientifically justify your read-across hypothesis.

0.1.1.2. Read-across hypothesis contradicted by existing data

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

21 The observation of differences in the toxicological properties between the source substance(s) and the Substance would contradict the hypothesis that the properties of the Substance can be predicted from the data on the source substances. An explanation why such differences do not affect the read-across hypothesis must be provided and supported by scientific evidence.

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

23 However, the results of the information obtained with the insoluble source substances such as lanthanum carbonate or lanthanum oxide vary from the ones obtained with the target. Specifically, an OECD 408 study with Lanthanum carbonate in the dossier, found no adverse treatment-related effects up to the highest dose used in the study (974.2 mg/kg bw/d for males and 1489 mg/kg bw/d for females). Also, a 3-generation study with Lanthanum oxide reported no effects up to the highest dose (91.8 mg/kg bw/d). By contrast, in a one generation study with lanthanum chloride in the dossier, a LOAEL of 10 mg/kg bw/day (nominal) was determined based on neurological assessment: more jerking and freezing behaviour, less vigorous in visual placing response. A developmental study with Lanthanum chloride also found deficits in the domains of neurobehavioral development, brain chemistry and learning and memory abilities.

24 In your comments to draft decision you argue that the effects highlighted above do "*not demonstrate* […] *neurobehaviour, memory or brain chemistry effects derive from ingestion of Lanthanum chloride anhydrous".* You consider irritiation of the stomach as the likely reason for the observed effects*.* You conclude that *"this is certainly not a sufficient basis*

for wholesale rejection of the read-across case, particularly as it is reinforced by the results of [redacted] *2019*".

25 ECHA observes that none of the provided studies with lanthanum chloride show evidence of stomach irritation. Furthermore, Lanthanum chloride is not classified as irritating to the skin. As such, your assumption that the neurotoxicity effects are due to stomach irritation is speculative. In addition, the relevance of the study of [redacted] 2019 to the conditions and effects *in vivo* is not explained.

26 In your comments to draft decision you also note that "*studies conducted on more soluble Lanthanum salts- such as Lanthanum chloride anhydrous- present a "worst case scenario" in terms of toxicological effects of less soluble Lanthanum Salts. The use of a more soluble Lanthanum Salt as a reference point ensures that there will be more lanthanum cations in solution*". ECHA considers that this could indeed explain the observed difference in toxicity between the soluble and insoluble lanthanum compounds.

27 The available set of data on the Substance and on the source substances indicate differences in the toxicological properties of the substances. This contradicts your read-across hypothesis whereby the Substance and source substances cause the same type of effect(s). However, you have not supported and scientifically justified why such differences in the toxicological properties do not affect your read-across hypothesis.

0.1.1.3. Adequacy and reliability of source studies

28 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.

Specific reasons why the studies on the source substances do not meet these criteria are explained further below under the applicable information requirement sections 8.4.1., 8.7.1., and 8.7.3. Therefore, no reliable predictions can be made for these information requirements.

0.1.1.4. Lack of relevance of the supporting information

29 Annex XI, Section 1.5. requires that whenever grouping and 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.

30 According to the Guidance on IRs and CSA, Section R.6.2.2.1.f., "it is important to provide supporting information to strengthen the rationale for the read-across approach. Thus, in addition to the property/endpoint being read across, it is also useful to show that additional properties, relevant to the endpoint, are also (qualitatively or quantitatively) similar between the source and target chemicals".

31 In your comments you refer to OECD TG 105 and OECD 29 T/D studies as being adequate and supportive for your read-across. More specifically:

- to the draft decision argument that "*information characterising the rate and extent of the (bio)transformation/dissolution of the Substance and of the source*

substance(s) is necessary" you argue "*that information was set out in the Dossier, which included the full suite of OECD 105 studies conducted when the original dossier for the Lanthanum salts were submitted*";

- you state that "*the draft decision should have required an OECD 29 T/D test for Lanthanum chloride anhydrous. ECHA has not requested an OECD 29 test for Lanthanum chloride anhydrous or Lanthanum nitrate. However, in the draft decision issued on the same day, it has requested OECD 29 tests for Lanthanum carbonate, Lanthanum oxide, Lanthanum hydroxide and Lanthanum fluoride*";
- you state that "*it would be disproportionate and wasteful to conduct all of the other tests requested in the DD without first obtaining the results of the OECD 29 tests*".

32 However, OECD TG 29 Test Guidance is designed to determine the rate and extent to which metals (which in their elemental state are not soluble in water) and sparingly soluble metal compounds can produce soluble available ionic and other metal-bearing species in aqueous media under a set of standard laboratory conditions representative of those generally occurring in the environment. Once determined, this information can be used to evaluate the short-term and long-term aquatic toxicity of the metal or sparingly soluble metal compound from which the soluble species came. You did not explain why such information is adequate for your read-across hypothesis and can translate directly to information on dissolution under physiologically relevant conditions.

33 Regarding your claim that "*the full suite of OECD 105 studies conducted when the original dossier for the Lanthanum salts were submitted*", the current dossier contains only one OECD TG 105 study for Lanthanum chloride and the read-across justification in the dossier did not make any supporting reference to either OECD TG 105 nor OECD TG 29 studies. Furthermore, you did not explain why the OECD TG 105 studies provide an adequate information allowing to infer the rate and extent of the (bio)transformation /dissolution.

34 Accordingly, this information is not considered as relevant to support your read-across hypothesis and you have not provided supporting information to scientifically justify the read-across explanation for prediction of properties.

0.1.2. Conclusion on the read-across approach

35 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.

0.2. Assessment of weight of evidence adaptations

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

- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Pre-natal developmental toxicity study in a second species (Annex X, Section 8.7.2.)

37 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.

38 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.

39 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.

40 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.

41 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.

42 In spite of this critical deficiency, common to all information requirements under consideration, ECHA has nevertheless assessed the validity of your adaptation.

43 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

44 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. In vitro gene mutation study in bacteria

45 An in vitro gene mutation study in bacteria is an information requirement under Annex VII, Section 8.4.1.

1.1. Information provided in the dossier

46 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 471 (1992) with the analogue substance Lanthanum nitrate 6*H2O, CAS number 6487-39-4.

1.2. Assessment of the information provided in the dossier

1.2.1. Read-across adaptation rejected

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

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

48 To fulfil the information requirement, a study must comply with OECD TG 471 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the test is performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101);
b) 2-Aminoanthracene should not be used as the sole indicator of the efficacy of the S9-mix.;
c) the number of revertant colonies per plate for the concurrent negative control is inside the historical control range of the laboratory.

49 However, the following specifications are not according to the requirements of the OECD TG 471:

a) the test was performed with the strains *S. typhimurium* TA100, TA1535, TA97, TA98 (i.e., the strains *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102 are missing);
b) 2-Aminoanthracene was used as the sole indicator of the efficacy of the S9-mix;
c) no information whether the number of revertant colonies per plate for the concurrent negative control is inside the historical control range of the laboratory since the historical control range of the laboratory was not reported.

50 In the comments to the draft decision, in relation to point a) above, you state that "*the missing strain is only detecting oxidative damage. As Lanthanum La3+ ions are known not to act as an oxidizing agent the missing strain would not contribute essential information at all.*" However, you have not provided any data to substantiate this claim.

51 Based on the above, the information provided does not cover the key parameters required by the OECD TG 471. Therefore, the information requirement is not fulfilled.

1.3. Information provided in your comments on the draft decision

52 In the comments to the draft decision you disagree with the request. You state that a "*weight of evidence approach using data from Lanthanum chloride, acetate, oxide hydroxide or fluoride shows that Lanthanum chloride is negative towards an in-vitro gene mutation study in bacteria.*"

53 However, none of these studies were provided in the dossier to support your weight of evidence for this endpoint.

54 Therefore, while ECHA understand that you intend to invoke a weight of evidence approach for this information requirement, this strategy relies essentially on data which is yet to be provided, therefore no conclusion on the compliance can currently be made with this intended approach.

1.4. Specification of the study design

To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471, 2020) is considered suitable.

2. Growth inhibition study aquatic plants

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

2.1. Information provided

56 You have provided:

(i) an OECD 201 study (1995) with the analogue substance Lanthanum chloride, hydrate, EC No. 640-503-8. For the purpose of hazard assessment, this Substance is considered equivalent to the Substance, the only difference being the degree of hydration.
(ii) an ISO 8692 study (2010) with the Substance
(iii) a non-guideline study type (1965) on *Chlorella vulgaris* with the Substance
(iv) a non-guideline study type (2005) on *Chlorella autotrophica* with the Substance
(v) a non-guideline (2002) on duckweed (*Lemna minor* L.) with the analogue substance Lanthanum chloride, hydrate, EC No. 640-503-8.

2.2. Assessment of the information provided

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

57 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:

58 Characterisation of exposure

a) if the concentration of the test material has not been maintained within ±20 % of the nominal or measured initial concentration throughout the test, results must be based on the geometric mean of measured concentrations during exposure or on a model describing the decline of the concentration of the test material over the exposure period;

59 Reporting of the methodology and results

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

60 Your registration dossier provides an OECD TG 201 study showing the following:

61 Characterisation of exposure

a) the concentrations of the test material were not detectable for the lower two tested concentrations and 7.77, 31.1 and 34.9 mg/l for remained three tested concentrations at the end of the test. Therefore, exposure was not maintained within ± 20 % of nominal or measured initial concentration throughout the test. It is unclear if the reported values correspond to either the geometric mean of measured concentrations during exposure or a model describing the decline of the concentration of the test material over the exposure period;

62 Reporting of the methodology and results

b) 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;
c) tabulated data on the algal biomass determined daily for each treatment group and control are not reported;
d) on the analytical method adequate information, i.e. analytical method and conditions and performance parameters of the method are not reported. The results of the analytically determined exposure concentrations at the beginning and the end of the test are provided.

63 Based on the above, ECHA considers that:

- there is a critical methodological deficiency resulting in the rejection of the study results. More specifically, due to the lack of information on the model describing the decline of the concentration of the test material over the exposure period and on the analytical information, the reliability of the effect value reported cannot be assessed.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, you have not provided measured biomass data. 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.

64 Therefore, the specifications of OECD TG 201 are not met.

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

65 To fulfil the information requirement, a study must comply with ISO 8692 (Article 13(3) of REACH). Therefore, the following specifications must be met:

66 Characterisation of exposure

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

67 Reporting of the methodology and results

b) the test conditions are reported (*e.g.*, composition of the test medium, test temperature, test species, biomass density at the beginning of the test);
c) the methods used to prepare stock and test solutions are reported;
d) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

68 Your registration dossier provides an ISO8692 study showing the following:

69 Characterisation of exposure

a) no analytical monitoring of exposure was conducted;

70 Reporting of the methodology and results

b) on the test conditions, you have not specified, test temperature, test pH and total hardness.
c) on the test procedure, you have not specified the methods used to prepare stock and test solutions;
d) tabulated data on the algal biomass determined daily for each treatment group and control are not reported.

71 Based on the above, ECHA considers that:

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the exposure concentration was not analytically verified and therefore the reliability of the effect value reported cannot be confirmed.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, you have not provided measured biomass data. Therefore, it is not possible to verify whether the validity criteria of the ISO 8692 were met and to verify the interpretation of the results of this study.

72 Therefore, the specifications of ISO 8692 are not met.

2.2.3. The provided studies (iii) and (iv) do not meet the specifications of Guidance on IRs and CSA

73 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 growth inhibition on algae the following specifications must be met:

74 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;

75 Characterisation of exposure

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

76 Reporting of the methodology and results

c) the test design is reported (*e.g.*, number of replicates, number of test concentrations and geometric progression used);
d) the test conditions are reported (*e.g.*, composition of the test medium, test temperature, test species, biomass density at the beginning of the test);
e) the methods used to prepare stock and test solutions are reported;
f) 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;
g) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

77 Your registration dossier provides the studies (iii) and (iv) showing the following:

78 Key parameter to be measured

a) for the study (iii) you provide a NOEC value of 4.1 mg/l based on biomass. For study (iv) you report an EC50 (96h)=4.052 mg/l based on biomass.

79 Characterisation of exposure

b) no analytical monitoring of exposure was conducted for any of the studies (iii) and (iv);

80 Reporting of the methodology and results

c) on the test design, you have not specified number of replicates for study (iii);
d) on the test conditions, you have not specified biomass density at the beginning of the test for any of the studies (iii) and (iv);
e) on the test procedure, you have not specified the methods used to prepare stock and test solutions for any of the studies (iii) and (iv);
f) the method used to determine algal biomass is not reported for study (iii). For study (iv) you report that algal biomass was determined using a spectrophotometer. 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;
g) tabulated data on the algal biomass determined daily for each treatment group and control are not reported;

81 Based on the above,

- the information provided in studies (iii) and (iv) do not cover the key parameter required by non-standard ecotoxicity tests on algae and aquatic plants. More specifically the values reported in both studies are based on biomass only while the required endpoint is growth rate inhibition.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically,
    - the exposure concentrations were not verified analytically and therefore the reliability of the results cannot be assessed.
    - you have not provided adequate information on the method used to determine algal biomass, on the measured biomass data and adequate information on the test design and procedure for any of the studies. 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

these studies.

82 Therefore, the specifications set out in Guidance on IRs and CSA, Section R.7.8.4.1, for the evaluation of data from non-standard ecotoxicity tests on algae are not met.

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

83 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:

84 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.

85 Characterisation of exposure

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

86 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.

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

88 Key parameter to be measured

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

89 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.

90 Reporting of the methodology and results

c) no tabulated data on the biomass is provided.

91 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.

92 Therefore, the specifications set out 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 are not met.

2.3. Assessment of the information provided in your comments on the draft decision

93 In your comments to the draft decision you do not agree to perform the study. You state that "*the test is technically not feasible as the neutral pH is causing a formation of poorly soluble hydroxide oxide forms*". ECHA understands that you intend to adapt this information requirement on the basis of Annex XI, Section 2.

2.3.1. Adaptation under Annex XI, Section 2 is rejected

94 According to Annex XI, Section 2, a study may be omitted if it is technically not feasible to conduct because of the properties of the substance. The guidance given in the test methods referred to in Article 13(3), in this case OECD TG 201, more specifically on the technical limitations of a specific method, shall always be respected.

95 The OECD TG 201 provides in particular that this test is applicable to substances that may affect the availability of nutrients or minerals in the test medium. For testing such substances certain modifications of the procedure mentioned in OECD TG 201 may be required.

96 You claim that the Substance forms "*poorly soluble Lanthanum phosphate hydrates and thus* [leading] *to nutrients depletion and subsequently reduced growth rate"*. Therefore, you consider testing according to OECD 201 is not technically feasible.

97 Your claim does not provide an objective demonstration supported by adequate evidence that the Substance cannot be tested using the OECD TG 201. In addition, you do not provide any justification or supporting information as to why the modifications mentioned in OECD TG 201 could not be applied.

98 Therefore, your adaptation is rejected.

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

Reasons related to the information under Annex VIII of REACH

3. In vitro gene mutation study in mammalian cells

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

3.1. Triggering of the information requirement

101 Your dossier contains (1) a negative result for in vivo micronucleus study, and (2) no data or inadequate data for in vitro gene mutation study in bacteria.

102 The in vitro gene mutation study in bacteria provided in the dossier is rejected for the reasons provided in Request 1.

103 The result of the Request 1 will determine whether the present requirement for an in vitro mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

104 Consequently, you are required to provide information for this information requirement if the in vitro gene mutation study in bacteria provides a negative result.

3.2. Information provided to fulfil the information requirement

105 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 476 (2005) with the analogue Lanthanum carbonate, CAS Number 587-26-8

106 Your registration dossier also contains the following *in vivo* study:

(ii) an OECD 486 (2005) with the Substance

107 ECHA understands that this information is provided as an attempt to adapt this information requirement under Annex VIII, Section 8.4.3., Column 2.

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

3.2.1. The read-across adaptation relating to study (i) is rejected

109 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.

110 In the comments to the draft decision, you disagree to conduct the requested study and propose to adapt the information requirement using a weight of evidence under Annex XI, Section 1.2 using data from other insoluble lanthanum analogues. We take note of your intention. However, this strategy relies essentially on data which is yet to be provided, therefore, no conclusion on the compliance can currently be made with this intended approach.

111 Concerning the data that you claim you will submit, we point out that the proposed analogues are insoluble substances. As explained in Section 0.1, we consider the data on insoluble substances not acceptable for reading across to the properties of the Substance.

112 Therefore, the provided study cannot be considered a reliable source of information.

3.2.2. The provided adaptation relating to study (ii) does not meet the criteria of Annex VIII, Section 8.4.3., Column 2

113 Under Annex VIII, Section 8.4.3., Column 2, the study may be omitted if adequate data from a reliable in vivo mammalian gene mutation test are available. The Guidance on IRs and CSA, Section R.7.7.6.3. clarifies that the in vivo study must be a Transgenic Rodent Somatic and Germ Cell Gene Mutation Assay (TGR), performed according to the OECD TG 488. This test investigates gene mutations using reporter genes.

114 The study (ii) is described as a UDS test. This is an indicator test that detects some DNA repair mechanisms (measured as unscheduled DNA synthesis in liver cells). However, it does not provide direct evidence of mutation as the TGR. According to the Guidance on IRs and CSA, Section R.7.7.6.3. (page 571-572), a negative result in a UDS assay alone is not a proof that a substance does not induce gene mutations. Moreover, the Guidance also clarifies that while a positive result in the UDS assay can indicate exposure of the liver DNA and induction of DNA damage by the substance under investigation, it is not sufficient information to conclude on the induction of gene mutation by the substance.

115 In the comments to the draft decision, you disagree with the request and provided the following justification: "*the study according to OECD 486 is not conclusive alone, but by providing additional data derived from an existing OECD 474 (Mammalian Erythrocyte Micronucleus Test) with a negative result, the combination of both studies will fulfil the information requirements.* [You] *will provide relevant data with the next dossier up-date*."

116 In your comments, you invoke data derived from an existing OECD 474 (Mammalian Erythrocyte Micronucleus Test) to supplement the information available for the in vitro gene mutation in mammalian cells endpoint. However, an OECD 474 is a study providing information fulfilling data requirement for cytogenicity but does not inform on gene mutation in mammalian cells and cannot mitigate the explained deficiencies for this endpoint.

117 The study (ii) is not a Transgenic Rodent Somatic and Germ Cell Gene Mutation Assay.

118 Therefore, the requirements of Annex VIII, Section 8.4.3., Column 2 are not met and your adaptation is rejected.

119 The study is not adequate for the information requirement and is therefore rejected.

3.3. Specification of the study design

120 To fulfil the information requirement for the Substance, either the in vitro mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

4. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days)

121 Annex VIII, Section 8.6.1., Column 2 provides that an experimental study for this information requirement is not needed if a reliable sub-chronic (90 days) or chronic toxicity study is available.

122 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 7). According to Annex VIII, Section

8.6.1., Column 2 and to prevent unnecessary animal testing, a short-term toxicity study (28 days) does not therefore need to be conducted.

123 In the comments to the draft decision you disagree with the request and you provide the following justification: "*Due to the availability of four repeated dose studies on Lanthanum chloride as well as on Lanthanum carbonate with a duration of 28d resp. of 90d suitable data for the endpoint(s) are available*."

124 You refer in your comments to two 28-day oral uptake studies performed on Lanthanum chloride and Lanthanum carbonate where the plasma concentration of Lanthanum after administration of comparable doses was found to be similar. However, these studies were not provided in the dossier, neither in the repeated dose toxicity endpoint nor in the toxicokinetics section of IUCLID. Therefore, this claim cannot be evaluated.

125 As explained in Section 0.1. of this draft decision, on the basis of the information currently provided in the dossier, the read across to insoluble salts cannot be accepted and thus the information requirement for sub-chronic (90 days) toxicity is not fulfilled. Therefore, ECHA maintains that a reliable sub-chronic (90 days) toxicity study (see request 7) must be provided.

126 Because you still must comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to submit a justification for the adaptation provided in Column 2 of that provision.

5. Screening for reproductive/developmental toxicity

127 A screening for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1., if there is no evidence from analogue substances, QSAR or in vitro methods that the substance may be a developmental toxicant.

5.1. Information provided

128 You have adapted the following standard information requirements by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2. In that respect, you have submitted the following sources of information:

(i) a 3-generation study (1975) with the Lanthanum oxide
(ii) a one-generation study (2000) with the Substance

5.2. Assessment of the information provided

129 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.

130 Relevant information that can be used to support weight of evidence adaptation for the information requirement of Annex VIII, Section 8.7.1. includes similar information that is produced by the EU B.63/OECD TG 421 or EU B.64/OECD TG 422 with a design as specified in this decision. OECD TG 421/422 require the study to investigate the following key elements:

1) sexual function and fertility,
2) toxicity to offspring, and
3) systemic toxicity.

5.2.1. Sexual function and fertility

131 Sexual function and fertility on both sexes must include information on mating, fertility, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, organ weights and histopathology of reproductive organs and tissues, litter sizes, nursing performance and other potential aspects of sexual function and fertility.

132 None of the studies provide information on gestational length, maintenance of pregnancy (abortions, total resorptions), parturition, organ weights and histopathology of reproductive organs and tissues, oestrus cyclicity, sperm count and analysis, hormone levels and nursing performance. However, the source of information (i) may provide relevant information on mating, fertility, lactation and litter size.

133 In any case, the reliability of these sources of information is significantly affected by the following deficiency:

5.2.1.1. The provided studies do not meet the specifications of the applicable test guidelines

134 To inform on the screening for reproductive/developmental toxicity, a 3-generation study (source of information i) a one-generation study (source of information ii) must normally follow the specifications of EU B.63/OECD TG 421 or EU B.64/OECD TG 422. Therefore, the following specifications must be met:

a) the highest dose level aims to induce toxicity or aims to reach the limit dose;
b) at least 10 male and 12-13 female animals are included for each dose and control group;
c) the exposure duration is at least four weeks for males, including a minimum of two weeks prior to mating, and approximately 63 days for females to cover premating, conception, pregnancy and at least 13 days of lactation;
d) food consumption is measured at least weekly;
e) thyroid hormone levels are measured;
f) Examination of parameters for sexual function and fertility such as /those for mating and fertility/duration of gestation, parturition, lactation and weight and histopathology of reproductive organs and tissues
g) Monitoring of oestrus cycles
h) Examination of offspring parameters such as /number and sex of pups/stillbirths and live births/gross abnormalities/pup body weight/litter weight/anogenital distance/number of nipples/areolae in male pups
i) Functional observations such as sensory reactivity to stimuli/assessment of grip strength/assessment of motor activity
j) Haematological examinations and clinical biochemistry
k) histopathology of reproductive organs and tissues is performed, and the presence or absence, incidence and severity of abnormalities is evaluated.

135 However, these sources of information show the following:

a) The highest dose level in the studies (i) and (ii) did not induce any systemic 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 421/422 and ECHA Guidance R7a.
b) The study (i) was conducted with 16 pregnant females but 8 males for each test group. Study (ii) was conducted with 10, 7 and 12 pregnant females for control, low and mid-dose and high dose respectively and no dosed males. The statistical power of the information provided is not sufficient because it does not fulfil the criterion of at least 10 male (both studies) and 12-13 female animals for each test group (study (ii)).

c) In the study (i) you have provided, it is not clear if the P0 males were dosed before mating or the exposure started after mating. In the study (ii) the males were not dosed. Therefore it does not fulfil the criteria set in EU B.63/OECD TG 421 or EU B.64/OECD TG 422.
d) In both studies, monitoring of food consumption was not performed.
e) In both studies, the thyroid hormone assessment (P0 and F1) was not performed.
f) In the study (ii) you have provided, the functional fertility has not been examined. In both studies essential information such as duration of gestation, parturition, and weight and histopathology of reproductive organs and tissues is missing.
g) In both studies, oestrus cyclicity has not been analysed.
h) In the studies you have provided, offspring parameters such as number and sex of pups, stillbirths and live births, pup body weight, litter weight, anogenital distance, number of nipples, areolae in male pups missing.
i) The study (i) does did not include functional observations.
j) In the study (ii) you have provided, investigations for clinical chemistry and haematology has not been performed, and it is limited only to few parameters in the study (i) (erythrocyte and leukocyte count, hemoglobin concentration, packed cell volume, serum protein, albumin, alpha-globulin, beta-globulin, gamma-globulin).
k) In both studies the histopathology of the reproductive organs and tissues has not been performed.

136 Based on the above, the studies (i) and (ii) do not provide an adequate and reliable coverage of the key parameter(s) addressed by the OECD TG 422.

5.2.1.2. Rejected read-across

137 The source of information (i) concerns data produced with an analogue substance. 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.

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

139 The deficiencies affecting the reliability of these sources of information are so significant that these sources of information could not contribute to the conclusion on the key parameter investigated by the study normally required.

140 In your comments on the draft decision, you indicate your intention to provide an improved read-across justification and a study on lanthanum acetate in a future update of your registration dossier. However, you do not provide specific information addressing the issues identified above.

5.2.2. Toxicity to offspring

141 Information on toxicity to offspring must include information on pre- and perinatal developmental toxicity reflected by litter sizes, postimplantation loss (resorptions and dead foetuses), stillborns, and external malformations, postnatal developmental toxicity reflected by survival, clinical signs and body weights of the pups (or litters), and other potential aspects related to pre-, peri- and postnatal developmental toxicity observed up to postnatal day 13.

142 The sources of information (i) and (ii) provide information on litter sizes, on peri- and postnatal toxicity up to postnatal day 13 (survival, clinical signs and body weights of pups). The source of information (i) provides information on the external malformations and the

source (ii) provides information on the neurotoxicity toxicity to offspring. None of studies provide information on postimplantation loss (resorptions and dead foetuses) and stillborns.

143 Furthermore, as indicated above under sexual function and fertility, the deficiencies affecting the reliability of sources (i) and (ii) are so significant that these sources of information could not contribute to the conclusion on the key parameter investigated by the study normally required.

5.2.3. Systemic toxicity

144 Information on systemic toxicity include clinical signs, survival, body weights, food consumption, haematology, clinical chemistry, organ weights and histopathology of non-reproductive organs and other potential aspects of systemic toxicity in the parental generation up to postnatal day 13.

145 The sources of information (i and ii) provide some information on systemic toxicity such as clinical signs, survival, body weights. Study (i) provides information on hematology, clinical chemistry and study (ii) on brain weight.

146 However, information on the following aspects are missing: food consumption, organ weights (except for brain weight provided in study (ii)) and histopathology of non-reproductive organs.

147 Furthermore, as indicated above under sexual function and fertility, the deficiencies affecting the reliability of sources (i) and (ii) are so significant that these sources of information could not contribute to the conclusion on the key parameter investigated by the study normally required.

5.2.4. Conclusion on the weight-of-evidence adaptation

148 In summary, the sources of information (i) to (ii) provide limited relevant information on sexual function and fertility, toxicity to offspring and systemic toxicity. However, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement for screening for reproductive/developmental toxicity endpoint.

In the comments to the draft decision, you do not comment on ECHA's findings described above. Nevertheless, you state generally that the sources of information "*do address the essential elements of those tests, as is required for WoE adaptation".*

149 In your comments, you also indicate your intention to refer to an OECD 422 study on Lanthanum acetate and two 28-day oral uptake studies performed on Lanthanum chloride and Lanthanum carbonate to consolidate your adaptation.

150 ECHA takes note of your intention to submit further sources of information for this information requirement. As indicated in your comments, this strategy relies essentially on data which is yet to be submitted, therefore no conclusion on the compliance can currently be made.

151 Regarding the adequacy of the weight of evidence approach, as already explained in this issue of the draft decision, the relevant information that can be used to support weight of evidence adaptation for the information requirement of Annex VIII, Section 8.7.1. should be similar to the information that is produced by the OECD TG 421 or OECD TG 422 with a design as specified in this decision. Nevertheless, as explained under 4.2.1.1., the deficiencies affecting the reliability of sources (i) and (ii) are so significant that these sources of information could not contribute to the conclusion on the key parameter investigated by the study normally required.

152 It is not possible to conclude, based on any source of information alone or considered together, on the information requirement for screening for reproductive/developmental toxicity. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

5.3. Specification of the study design

153 A study according to the test method EU B.64/OECD TG 422 must be performed in rats.

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

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

6. Short-term toxicity testing on fish

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

6.1. Information provided in your dossier

157 You have adapted this information requirement by using Column 2 of Annex VII, Section 9.1.3. To support the adaptation, you have provided following justification: "*Data on chronic toxicity to fish are available for Lanthanum trichloride hydrate, thus in accordance with column 2 of REACH Annex VIII no testing on short-term toxicity to fish is required*".

6.2. Assessment of the information provided in your dossier

6.2.1. The provided adaptation does not meet the criteria of Annex VIII, Section 9.1.3., Column 2

158 Under Section 9.1.3., Column 2, second indent, Annex VIII to REACH, the study may be omitted if a long-term aquatic toxicity study on fish is available.

159 Your registration dossier provides an OECD 204 (1995) study with the analogue substance Lanthanum chloride, hydrate (EC 640-503-8).

160 As explained in Request 9 below, the provided study is not considered a long-term test

161 Therefore, your adaptation is rejected.

6.3. Information provided in your comments on the draft decision

162 In your comments on the draft decision, you state that you do not agree to perform the study. You state that you "*will enhance the dossier by using the already provided OECD 204 on the substance together with OECD 203 study on Lanthanum oxide and Nitrate*". ECHA understands that:

- you may intend to use the available OECD 204 study with the substance to fulfil this information requirement (Short-term toxicity testing on fish, Annex VIII to REACH, Section 9.1.3.), and
- you may intend to adapt this information requirement by means of grouping and read-across according to Annex XI, Section 1.5, of the REACH Regulation.

163 ECHA takes note or your intentions to submit a read-across approach for this information requirement. As the information in your comments is not sufficient for ECHA to make an assessment, no conclusion on the compliance can currently be made.

164 ECHA has assessed the adequacy of using the available OECD 204 study further below.

6.4. Assessment of the information provided in your comments on the draft decision

6.4.1. The OECD 204 study provided in your registration dossier does not meet the specifications of the test guideline OECD TG 203.

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

Key parameter to be measured

a) the concentration of the test material leading to the mortality of 50% of the juvenile fish at the end of the test (96h) is estimated;

Characterisation of exposure

b) in *semi-static tests, test concentrations are measured at least twice over one exposure period (before and after renewal of test solutions). If the concentrations of the test material are expected to decline by more than 20%, analytical monitoring is conducted on all test concentrations with additional determinations on the other exposure period(s);*

Reporting of the methodology and results

c) the size (weight and length) of the tested animal must be reported;

d) 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;

166 Based on the information available in your registration dossier, in the available OECD 204 study:

Key parameter measured

a) the concentration of the test material leading to the mortality of 50% of the juvenile fish at 96h was not estimated;

Characterisation of exposure

b) the test was conducted under semi-static conditions and exposure concentrations were measured:

- on day 0 for all test concentrations,
- at the first renewal for the concentrations representing 4, 20 and 100% (v/v) of the saturated solution,
- on day 7 for the concentrations representing 4, 20 and 45% (v/v) of the saturated solution,
- on day 14 for the concentrations representing 4, 9 and 20% (v/v) of the saturated solution, and
- on day 21 at 4, 9 and 20% (v/v) of the saturated solution.

You also state that "t*he measured concentrations indicated an exponential decline of actual concentrations during the first 48 h of each period of renewal*". Therefore, the exposure concentrations did not remain within ± 20 % of nominal but no additional determinations were made.

Reporting of the methodology and results

c) the mean size of fish was not reported.

d) 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;

167 Based on the above,

- the information provided does not cover the key parameter required by the OECD TG 203 and therefore the results of this study are not adequate for the purpose of classification and labelling and risk assessment.
- the available analytical monitoring data indicates that exposure concentrations were not maintained within ± 20 % of nominal during the first 48h of the test. Furthermore, no analytical data are available from 48h to 96 h. Therefore, the exposure of the test animal to the test material during the exposure phase relevant to the short-term toxicity to fish is not adequately characterised.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. Specifically, the mean size of fish was not reported and therefore it is not demostrared that the test was performed on juvenile fish as required by the OECD TG 203. In addition, tabulated data on mortalities and sub-lethal effects was not provided and therefore fish mortality after 96h cannot be determined.

168 On this basis, the OECD TG 204 from your dossier does not provide equivalent information to an OECD TG 203. Therefore, this study does not meet the information requirement and you remain responsible for complying with this decision by the set deadline.

Reasons related to the information under Annex IX of REACH

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

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

7.1. Information provided in your dossier

170 You have provided the following information on the Substance:

(i) A 28-d study (1992) with the Substance
(ii) A 90-d study (2007) with the Substance

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

(iii) An OECD 408 (2006) with the analogue Lanthancarbonat-octahydrat, EC 209-599-5

7.2. Assessment of the information provided in the dossier

7.2.1. The studies (i) and (ii) do not meet the specifications of the applicable test guidelines

172 To fulfil the information requirement, a study must comply with the OECD TG 408 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) highest dose level should aim to induce toxicity or reach the limit dose;
b) at least 10 male and 10 female animals for each test and control group;
c) dosing of the Substance daily for a minimum of 90 days;
d) clinical signs observed daily and functional observations week 11 or after, i.e. sensory activity, grip strength and motor activity assessments;
e) the oestrus cycle in females at necropsy;
f) terminal organ and body weights;
g) gross pathology as specified in paragraphs 43-46 of the test guideline;
h) full histopathology as specified in paragraphs 47-49 of the test guideline.

173 In studies (i) and (ii), the following specifications are not according to the requirements of the OECD TG 408:

a) no justification for the dose setting while the highest dose levels tested was 40 mg/kg bw/d, which is below the limit dose of the test guideline, and no adverse effect were observed (study (ii));
b) 9 males/ 9 females in each test and control group (study (ii));
c) an exposure duration of 28 days (study (i));
d) data on clinical signs (study (i) and functional observations are missing: nature, severity and duration (studies (i) and(ii));
e) data on oestrus cycle are missing (studies (i) and(ii));
f) data on terminal organ weights and organ/body weight ratios are missing (studies (i) and(ii));
g) data on gross pathology findings are missing: incidence and severity (studies (i) and(ii));
h) data on histopathology findings are missing: incidence and severity (studies (i)

and (ii)).

174 The information provided does not cover the key parameters required by the OECD TG 408.

7.2.2. Read-across adaptation rejected

175 The study (iii) is performed with the source substance Lanthancarbonat-octahydrat.

176 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.

177 Therefore, the information requirement is not fulfilled.

7.3. Information provided in your comments on the draft decision

178 In the comments to the draft decision you disagree with the request and invoke the data waiving according to Annex IX Section 8.6.2., Column 2: *"Reliable data on chronic studies are available, which cover the concerned route of exposure, an additional sub-chronic study is not necessary".* You disagree *"that a study per se will be rejected based on the fact that information are missing and in case the existing studies contain the required information, an up-date is always feasible as long as the information demanded can be provided. It is* [your] *understanding that that information can be scientifically combined in a weight of evidence approach in order to fulfil the data requirements".* [You] *will update newly conducted studies in the next dossier update*."

7.4. Assessment of the information provided in your comments on the draft decision

179 Annex IX Section 8.6.2., Column 2 specifies that a sub-chronic toxicity study (90 days) does not need to be conducted if a reliable chronic toxicity study is available, provided that an appropriate species and route of administration were used.

180 In your dossier no chronic studies are available and no robust study summary was provided in your comments. Therefore, it is not possible to assess if such a study would fulfil the information requirement.

181 Regarding the way the information can be combined in a weight of evidence, such an information should be similar to the information that is produced by the OECD TG 408, with a design as specified in this decision. However, as explained under 6.1.1., the deficiencies affecting the reliability of sources (i) and (ii) performed with the Substance are too significant and, when taken together, do not mitigate the identified deficiencies. For instance, both studies performed with the Substance are missing histopathology findings. Therefore no information on histopathology findings is available.

182 On this basis, the information requirements are not fulfilled, and you remain responsible for complying with this decision by the set deadline.

7.5. Specification of the study design

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

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

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

8. Pre-natal developmental toxicity study in one species

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

8.1. Information provided

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

(i) a developmental toxicity study (2006) with the Substance in rats
(ii) a one-generation study (2000) with the Substance in mice

8.2. Assessment of the information provided

188 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.

189 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.

8.2.1. Pre-natal developmental toxicity

190 Pre-natal developmental toxicity includes information after pre-natal 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).

191 The sources of information (i and ii) provide relevant information on growth.

192 However, the reliability of these sources of information is significantly affected by the following deficiencies:

193 To be considered compliant and to generate information concerning the effects of the Substance on pre-natal developmental toxicity, the study has to meet the requirements of OECD TG 414. Therefore, the following specifications must be met:

a) the highest dose level aims to induce toxicity or aims to reach the limit dose;
b) at least 20 female animals with implantation sites for each test and control group are included;
c) the exposure duration is at least from implantation until one day prior to scheduled caesarean section;
d) the dams are examined for any structural abnormalities, weight and histopathology of the thyroid gland, thyroid hormone measurements, gravid uterus weight, and uterine content;
e) the foetuses are examined for body weight, number and percent of live and dead foetuses and resorptions, sex ratio, external, skeletal and soft tissue alterations (variations and malformations), measurement of anogenital distance in all live rodent foetuses.

194 The studies (i) and (ii) are described as focusing on the neurodevelopmental effects of lanthanum. Furthermore, the following specifications are not according to the requirements of the OECD TG 414:

a) the highest dose levels tested in both studies was 40 mg/kg bw/d, which is below the limit dose of the test guideline, and no adverse effect were observed, and no justification for the dose setting;
b) Only 16 pregnant females for each test group were included in study (i). Only 10,

7 and 12 pregnant females for control, low and mid-dose and high dose respectively were included in study (ii);
In your comments on the draft decision, you state "*This is correct, as far as it goes. However, taking the two studies together offers a more than sufficient basis for WoE adaptation*". Nevertheless, since the required number of animals was set to ensure the statistical power in OECD TG 414, a lower number affects the study reliability. Adequate and reliable documentation is a mandatory condition for the weight of evidence adaptation. Thus, it is not appropriate to add up the insufficient number of animals from several studies to account for this parameter.

c) In the study (i), the maternal rats were exposed to lanthanum from gestation day 0 through postnatal day 20. From postnatal day 20, pups were exposed to Lanthanum until postnatal day 150. In the study (ii) the animals were exposed prior to conception, during gestation, and until 30 days postnatally;
In your comments you state that "[you do] *not understand why ECHA has concluded that this is insufficient. In any event it is certainly enough to take the two studies together as the basis for a WoE adaptation*". In relation to the exposure duration, ECHA clarifies that the reason for which the pups are sacrificed a day before caesarean section in the pre-natal developmental toxicity studies is to avoid the bias on the number of possibly malformed animals, due to canibalism and postnatal death. In the study (ii), you inform that the "*Litter size did not differ significantly between the groups [F(3, 32) = 0.33, p = 0.8 nor did the mortality rate of the pups due to cannibalism or death of unknown cause*". Nevetheless, this does not inform whether those pups showed or not malformations.

d) In both studies the weight and histopathology of the thyroid gland has not been examined in dams, thyroid hormone measurements have not been conducted in dams, gravid uterus weight has not been measured and uterine content has not been examined;

e) In both studies, the sex and body weight of the foetuses has not been examined, external, skeletal and soft tissue alterations (variations and malformations) have not been examined, number of resorptions and or dead foetuses have not been recorded, anogenital distance has not been measured in live foetuses.

195 The deficiencies affecting the reliability of sources (i) and (ii) are so significant that these sources of information could not contribute to the conclusion on the key parameter investigated by the study normally required.

196 In the comments to the draft decision you disagree with the request and argue that "*Taken together, they* [the studies] *provide a sufficient basis for a WoE adaptation. The essential elements of OECD 414 are addressed for pre-natal developmental toxicity*."

197 However, essential elements linked to the most severe deficiencies (the sex and body weight of the foetuses not being examined, external, skeletal and soft tissue alterations (variations and malformations) not being examined, number of resorptions and or dead foetuses not being recorded, anogenital distance not being measured in live foetuses) were not addressed in your comments.

198 Therefore, the information requirement is not fulfilled.

199 Maternal toxicity

200 Maternal toxicity includes information after gestational exposure on maternal survival, body weight and clinical signs and other potential aspects of maternal toxicity in dams.

201 The sources of information (i) and (ii) provide information on maternal toxicity. However, as indicated under pre-natal developmental toxicity above, the deficiencies affecting the reliability of sources (i) and (ii) are so significant that these sources of information could

not contribute to the conclusion on the key parameter investigated by the study normally required.

8.2.2. Maintenance of pregnancy

202 Maintenance of pregnancy includes information on abortions and/or early delivery as a consequence of gestational exposure and other potential aspects of maintenance of pregnancy.

203 The sources of information (i) and (ii) provide information on maintenance of pregnancy. However, as indicated under prenatal developmental toxicity above, the deficiencies affecting the reliability of sources (i) and (ii) are so significant that these sources of information could not contribute to the conclusion on the key parameter investigated by the study normally required.

8.2.3. Conclusion on weight of evidence

204 In summary, the sources of information (i-ii) provide relevant information on prenatal developmental toxicity, maternal toxicity, and maintenance of pregnancy. However, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement.

205 In the comments to the draft decision you disagree with the request and consider that: "*Request is arbitrary because not required for Lanthanum carbonate, oxide, hydroxide or nitrate where these same referenced studies were considered sufficient*".

206 ECHA clarifies that for lanthanum carbonate, oxide, and hydroxide this endpoint was fulfilled by prenatal and developmental toxicity studies performed with the substance registered in that dossier or another insoluble lanthanum compound. For lanthanum nitrate (Annex VIII) the endpoint was fulfilled with an OECD 422 with another soluble compound, lanthanum acetate. Thus, the studies provided for this information requirement in your dossier were not the basis for the decisions taken for the other substances.

207 In your comments to the draft decision, you also state that "*weight of evidence assessment should take account of the studies relied upon in the dossiers of the other (inorganic) Lanthanum salts*."

208 However, the draft decision is based on the data reported by you in your dossier. In addition, it is the exclusive responsibility of registrants to invoke adaptation and to ensure that their adaptation complies with the conditions set out in the REACH Regulation.

209 Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in OECD TG 414. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

8.3. Specification of the study design

210 A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[2] administration of the Substance.

9. Long-term toxicity testing on fish

[2] ECHA Guidance R.7a, Section R.7.6.2.3.2.

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

9.1. Information provided

212 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 No. 640-503-8.

9.2. Assessment of the information provided

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

213 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.

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

215 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.

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

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

Reasons related to the information under Annex X of REACH

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

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

10.1. Information provided

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

(i) a developmental toxicity study (2006) with the Substance in rats
(ii) a one-generation study (2000) with the Substance in mice

10.2. Assessment of the information provided

220 As explained under the request 8 of this draft decision, your adaptation based on a weight of evidence approach under Annex XI, Section 1.2. is rejected.

221 Therefore, the information you provided do not fulfil the information requirement.

222 In the comments to the draft decision, you indicate that you plan to address this information requirement/the deficiencies. However, in your comments you have not provided any new scientific information that could address the information requirement/the deficiencies.

223 On this basis the information requirement is not fulfilled.

10.3. Specification of the study design

224 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 8 in this decision).

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

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

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

The information requirement for an Extended one-generation reproductive toxicity study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the Sub-chronic toxicity study (90-day) requested in the present decision is provided; due to the fact that the results from the 90-day study is needed for the design of the EOGRTS.

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.

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 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 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]

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[3].

(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.

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

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[4].

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