EUROPEAN CHEMICALS AGENCY

Helsinki, 26 November 2018

Addressee: [redacted]

Decision number: CCH-D-2114447819-33-01/F
Substance name: neodymium oxide
EC number: 215-214-1
CAS number: 1313-97-9
Registration number: [redacted]
Submission number: [redacted]
Submission date: 29/06/2017
Registered tonnage band: 100-1000

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **Description of the analytical methods (Annex VI, Section 2.3.7.) on the registered substance;**

   - **Identification and quantification of the impurities**

2. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: OECD TG 424) in rats, and in accordance with paragraph 16 of OECD TG 424, the study protocol shall be combined with OECD TG 408, with the registered substance ;**

3. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) in a first species (rat or rabbit), oral route with the registered substance ;**

4. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with test material representative of the registered substance as specified in Appendix 1, section 4;**

5. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with test material representative of the registered substance as specified in Appendix 1, section 4;**

6. **Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4.; test method: Activated sludge, respiration inhibition test (carbon and ammonium oxidation), OECD TG 209) with test material representative of the registered substance as specified in Appendix 1, section 4.**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI to the REACH Regulation. To ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by ***3 December 2020***. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by **Claudio Carlon**, Head of Unit, Evaluation

[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

INFORMATION ON SUBSTANCE IDENTITY

In accordance with Article 10(a)(ii) of the REACH Regulation, the technical dossier must contain information on the identity of the substance as specified in Annex VI, Section 2 to the REACH Regulation. In accordance with Annex VI, Section 2 the information provided has to be sufficient to enable the identification of the registered substance.

1. Description of the analytical methods (Annex VI, Section 2.3.7.)

As indicated in section 4.2.1 of the 'Guidance for identification and naming of substances under REACH and CLP' (May 2017, Version 2.1), referred hereafter as the Guidance, a mono-constituent substance is a substance, defined by its quantitative composition which is proven by the spectroscopic and analytical information. X-Ray Diffraction (XRD), X-Ray Fluorescence (XRF) or Atomic Absorption Spectroscopy (AAS) are suitable method of analysis for an inorganic substance. Chapter 7.5 of the Guidance specifies further that the characteristic XRD or IR peaks identifying the mineral should be given together with a short description of the analytical method or bibliographical reference.

You have reported the Neodymium trihydroxide impurity in section 1.2 with concentration range [redacted]%, typically [redacted]%. In the remarks field of this impurity you state that "Detected by XRD analysis". The provided XRD diffractogram (as well as IR spectra) may be used to indicate the presence of this impurity; however, it cannot be used to confirm the content of this impurity as the method applied does not appear to be quantitative.

Therefore, your dossier does not have sufficient information to verify the reported composition of the registered substance and therefore its identity. Other quantitative analytical methods to confirm the concentration of the impurities should be provided.

In your comments on the draft decision you agreed to update the relevant section of the registration dossier to include the requested information.
Accordingly, you are required to provide the description of the analytical method used on the quantification of the Neodymium trihydroxide impurity(-ies) with sufficient accuracy to confirm the identity of the subtance.

The description shall be sufficient for the methods to be reproduced and shall therefore include details of the experimental protocol followed, any calculation made and the results obtained. In case of the XRD-based quantification please indicate the method applied (internal / external standard, whole pattern / Rietveld) and provide description accordingly.

You shall ensure that the analytical data provided on the quantification of the substance is *consistent with the composition and identity reported for the substance.*

As for the reporting of the data in the registration dossier, the information should be attached in IUCLID section 1.4.

INFORMATION ON TOXICITY

2. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

You have not provided any study record of a sub-chronic toxicity study (90 day) in the dossier that would meet the information requirement of Annex IX, Section 8.6.2.

You have sought to adapt this information requirement. You provided the following justification for the adaptation: "*In accordance with Section 1 of Annex IX a subchronic toxicity study, as required under Section 8.6.2. of Annex IX does not appear to be scientifically necessary. The existing oral data is considered to adequately address the repeated dose toxicity endpoint and a further 90-day study is regarded as unnecessary*".

However, ECHA notes that your adaptation does not meet either the specific rules for adaptation of Annex IX, Section 8.6.2., column 2 or any of the general rules for adaptation of Annex XI. You have not provided any justification for why the existing data is adequate for the information requirement for a sub-chronic toxicity study.

In the technical dossier you have provided a study record for a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD TG 422). However, this study does not provide the information required by Annex IX, Section 8.6.2., because the exposure duration is less than 90 days and the number of animals examined per dose group for histopathology and clinical chemistry is significantly lower than in the 90 day sub-chronic toxicity study (OECD TG 408).

Therefore, your adaptation of the information requirement is rejected.

ECHA further notes that in an OECD TG 422 study performed on the registered substance, neurological effects were observed. In that particular study, there was an increase in female animals in the incidence of body held low or hunched in the arena and partial palpebral closure during Weeks 5 and 6 in animals dosed at 1000 mg/kg/day; these values were outside of the historical control range. In addition, in the detailed functional observations, there was in female animals a reduction in sectors crossed during Weeks 4 and 6 and number of rears noted in the arena during Week 6 in animals dosed at 1000 mg/kg/day; these values were outside of the historical control data. This information indicates that the neodymium oxide causes neurotoxicity, hence there is a concern for neurotoxicity of the registered substance.

ECHA notes that a sub-chronic toxicity study by the oral route is normally performed according to OECD TG 408. However, while the OECD TG 408 does include some examinations of neurological endpoints, these examinations alone may not be sufficient given the neurological effects identified in the previous study on neodymium oxide. ECHA notes that according to the ECHA guidance on information requirements and chemical safety assessment, Chapter R.7a, the OECD TG 424 is an appropriate study for confirmation or further examination of neurotoxicity identified in previous studies.

ECHA further notes that the OECD TG 424 study design allows for the combination of the neurotoxicity study with a sub-chronic toxicity study (90 days). Such a combined study allows for addressing the information gap in your dossier for a sub-chronic toxicity and addressing the concern for neurotoxicity, while minimising the use of animals.

Accordingly, the study protocol of the 90 day repeated dose toxicity study shall be performed according to method B.43 (or OECD 424) to evaluate neurotoxic effects, in combination with a standard 90-day repeated dose toxicity study (method B.26 or OECD 408).

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.5.4.2 - is the most appropriate route of administration. Moreover, the available oral study on neodymium oxide indicates a concern for systemic toxicity (more specifically, neurotoxicity) that requires further information on repeated dose toxicity by the oral route. Hence, the test shall be performed by the oral route.

According to the test method EU B.43/OECD 424 and EU B.26./OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

In your comments on the draft decision you agree to the request for a sub-chronic toxicity study (OECD TG 408), but you do not agree that the effects seen in the OECD TG 422 study would justify the sub-chronic toxicity study to be combined with OECD TG 424.

You suggest that "*Altogether, the alterations observed during functional clinical observations stem from decreased general state of single animals due to body weight loss and mis-gavage (or aspiration of test material) rather than substance-related neurotoxicity*"

For the body weight loss, you explain that "*At 300 mg/kg/day and above there was a dose-related decrease in group mean body weight gain during the lactation period only.*" ECHA notes that according to the OECD TG 422 study report, "*Females were treated for 2 weeks prior to mating, then through mating, gestation and until at least Day 4 of lactation (ca 6 weeks of treatment)*" and "*At levels up to 1000 mg/kg/day the group mean body weight gain for females prior to mating and throughout gestation were similar to Controls*".

ECHA considers that the decrease in body weight gain only during lactation period would not explain the neurological effects seen during the whole duration of the study.

As a general comment, you consider that "*It is not uncommon that during repeated-dose toxicity studies using gavage as the via of administration some mis-gavage can occur*". You further explain that this leads to deterioration of the well-being of the animals, manifested with clinical signs reflecting discomfort which can be interpreted as signs of neurotoxicity.

You state that "*In the OECD 422 study with neodymium oxide some clinical signs were observed in few animals in each group*". You further note that necropsy and histopathology findings (e.g. alveolar foamy macrophage accumulation) suggest that for some animals, at some point of the study, mis-gavage had occurred.

ECHA notes that this type of histopathological findings were recorded for controls as well as

treated animals, and that e.g. hunched posture was observed in both groups. However, the partial palpebral closure, and reduction in sectors crossed as well as number of rears noted in the arena were only observed in the treated animals, and ECHA considers that these neurological effects are treatment-related and not just a sign of discomfort due to possible mis-gavaging.

Therefore, you are required to carry out the following test using the indicated test method and the registered substance subject to the present decision: Neurotoxicity study in rodents (Annex IX, 8.6.2. REACH Regulation) in the rat, by the oral route for 90 days (method B.43 of Regulation (EC) No 440/2008 or OECD 424), and in accordance with paragraph 16 of OECD 424, the study protocol shall be combined with a repeated dose 90-day oral toxicity study (OECD 408).

Notes for your consideration

ECHA notes that a revised version of OECD TG 408 was adopted this year by the OECD. This revised version contains enhancements of certain endocrine disrupting relevant parameters. You should test in accordance with the revised version of the guideline as published on the OECD website for adopted test guidelines (https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788).

3. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "pre-natal developmental toxicity study" (test method EU B.31./OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a pre-natal developmental toxicity study in the dossier that would meet the information requirement of Annex IX, Section 8.7.2.
You have sought to adapt this information requirement. You provided the following justification for the adaptation: "*In accordance with Section 1 of Annex XI, the pre-natal developmental toxicity study, as required in Section 8.7.2 of Annex IX, does not appear scientifically necessary. No developmental effects were noted in an OECD 422 screening study and in the absence of any other reasonable grounds for concern there is considered to be no need to further investigate this endpoint*".

However, ECHA notes that your adaptation does not meet either the specific rules for adaptation of Annex IX, Section 8.7.2., column 2 or any of the general rules for adaptation of Annex XI; because a combined repeated dose toxicity study with the reproduction/developental toxicity screening test is not an adequate study to fulfill the information requirements for a pre-natal developmental toxicity study.

ECHA notes that in the technical dossier you have provided a study record for a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test"

(test method: OECD TG 422). However, this study does not provide the information required by Annex IX, Section 8.7.2. because it does not cover key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations. Therefore, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method EU B.31./OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid, ECHA concludes that testing should be performed by the oral route.

In your comments on the draft decision you agreed to conduct the requested study. Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: OECD TG 414) in a first species (rat or rabbit) by the oral route.

Notes for your consideration

ECHA notes that a revised version of OECD TG 414 was adopted this year by the OECD. This revised version contains enhancements of certain endocrine disrupting relevant parameters. You should test in accordance with the revised version of the guideline as published on the OECD website for adopted test guidelines (https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788).

INFORMATION ON ECOTOXICITY

4. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a long-term toxicity on aquatic invertebrates in the dossier that would meet the information requirement of Annex IX, Section 9.1.5.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.5., column 2. You provided the following justification for the adaptation:
"In accordance with point 9.1.5 of Column 2, specific rules for adaptation from Column 1, of Annex IX of REACH, the long-term testing on aquatic invertebrates study does not need to be conducted as the chemical safety assessment concludes that the substance is of no immediate concern to the environment. The available data are adequate for classification and labeling purposes and PBT assessment is not applicable for inorganic substances, so no further testing is required. Long term assays are required if there is a need to further investigate the impacts on aquatic organisms. Due to its extremely low water solubility (water solubility = 7.8 µg/L, RCC study N° B38856, 2008, GLP), it can be argued that neodymium oxide will not be bioavailable to aquatic organisms. Furthermore, in acute toxicity experiments, none of the tested species (i.e. fish, daphnids and algae) exhibited adverse effects, with L/EC50 values all superior to the solubility limit into water. Thus, due to the high insolubility of neodymium oxide and its absence of aquatic acute ecotoxicity, the long-term assay on aquatic invertebrates is not needed. "

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.5., column 2 because ECHA considers that there is a need to further investigate the effects on aquatic organisms.

You claim that the low solubility of the substance precludes bioavailability and argue that the lack of effects in the available short term tests is sufficient to conclude that further testing is not needed. ECHA notes that the measured solubility value of 7.8 ug/L indicates that there is some (albeit poor) solubility and consequently long term testing is appropriate for this substance. ECHA concludes that given the poor solubility of the substance the available short term tests are unreliable and the absence of toxicity in these short term tests is irrelevant. As there are no reliable short-term studies available on aquatic invertebrates or on fish for the registered substance, the Integrated testing strategy (ITS) outlined in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b (Section R.7.8.5 including Figure R.7.8-4) is not applicable in this case and long-term studies on both invertebrates and fish are required.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) *Daphnia magna* reproduction test (test method EU C.20. / OECD TG 211) is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5.

In your comments on the draft decision (DD) you stated that aquatic toxicity testing of the registered substance, a "*poorly water soluble rare earth compound*", would not produce meaningful data for classification and labelling and risk assessment due to difficulties related to dissolution of the test substance. You indicated that according to ECHA Guidance on the Application of the CLP Criteria (Version 5.0, July 2017) the preferred approach for classification is to compare acute and/or chronic Ecotoxicological Reference Values (ERVs) with concentrations of dissolved metal ions observed during a transformation/dissolution study. You therefore indicated that to complete the hazard assessment and to determine

the classification of the registered substance you will conduct an OECD 29 Transformation/Dissolution of Metals and Metal compounds in aqueous media study and compare the obtained concentration(s) of soluble metal ions in this study with ERVs on soluble neodymium salts.

ECHA agrees that ecotoxicity of most poorly soluble metal compounds is best assessed using data on the soluble metal ion, and that the approach described by you is appropriate for classification purposes as given in ECHA Guidance on the Application of the CLP Criteria (Version 5.0, July 2017). ECHA also agrees that generating data according to the OECD TG 29 is a prerequisite for the approach described by you. However, ECHA notes that transformation/dissolution data may be used to fulfil the standard information requirement of Annex VII, section 7.7., but on its own it cannot fulfil the present information requirement of long-term toxicity testing on aquatic invertebrates. ECHA further notes that no aquatic toxicity data obtained with the soluble neodymium salts is provided within your registration dossier nor in your comments.

Therefore, you need to provide the requested aquatic toxicity data generated with a test material representative of the registered substance, ie. with the soluble ion(s). If no data on long-term toxicity to aquatic invertebrates is available on soluble neodymium ion(s), such data need to be generated. If new ecotoxicity testing is initiated any advice provided in the specific guideline, OECD TG 211 in the present case, for testing of metals should be followed. Analytical monitoring of the exposure concentrations is required to demonstrate the concentration of the metal ion tested. You also need to provide a scientifically valid read-across justification (according to Annex XI, section 1.5.) on how the data you intend to use to fulfil the present information requirement relates to the whole substance, including, for instance, the counter-ion and any impurities. To fulfil the requirements of Annex XI section 1.5. the information provided needs to be useful for both hazard and risk assessment and for classification and labelling.

For classification purposes, you can use the approach described in ECHA Guidance on the Application of the CLP Criteria (Version 5.0, July 2017). Bearing in mind the requirement to cover the whole registered substance as given above, for hazard and risk assessment you need to follow the approach given for PNEC derivation and risk characterisation in ECHA Guidance on Information requirements and chemical safety assessment, Chapter R.10 (May 2008) and required by Annex I, section 3.3 of the REACH Regulation . Any substance specific considerations you may use in your hazard and risk assessment need to be fully justified and the approach chosen needs to cover the whole substance as registered.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit information generated with a test material representative of the registered substance subject to the present decision: Daphnia magna reproduction test (test method: EU C.20./OECD TG 211).

Notes for your consideration

Once results of the test on long-term toxicity to aquatic invertebrates are available, you shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation.

Due to the low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment*

(version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

5. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. Adequate information on Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.), or Fish, short-term toxicity test on embryo and sac-fry stages (Annex IX, 9.1.6.2.), or Fish, juvenile growth test (Annex IX, 9.1.6.3.) needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a long-term toxicity on fish in the dossier that would meet the information requirement of Annex IX, Section 9.1.6.1 / 9.1.6.2 / 9.1.6.3.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.6., column 2. You provided the following justification for the adaptation:
"In accordance with Column 2, specific rules for adaptation from Column 1, of REACH Annex IX, the long-term testing on fish study, listed under standard information requirement 9.1.6, does not need to be conducted as the chemical safety assessment concludes that the substance is of no immediate concern to the environment. The available data are adequate for classification and labelling purposes and PBT assessment is not applicable for inorganic substances, so no further testing is required. Long-term assays are required if there is a need to further investigate the impacts on aquatic organisms. Due to its extremely low water solubility (water solubility = 7.8 µg/L, RCC study N° B38856, 2008, GLP), it can be argued that neodymium oxide will not be bioavailable to aquatic organisms. Furthermore, in acute toxicity experiments, none of the tested species (i.e. fish, daphnids and algae) exhibited adverse effects, with L/EC50 values all superior to the solubility limit into water. Thus, due to the high insolubility of neodymium oxide, due to its absence of aquatic acute ecotoxicity and in accordance with the REACH principle intended to limit vertebrate testing, the long-term assay on fish is not needed".

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.6., column 2 because ECHA considers that there is a need to further investigate the effects on aquatic organisms.

You claim that the low solubility of the substance precludes bioavailability and argue that the lack of effects in the available short term tests is sufficient to conclude that further testing is not needed. ECHA notes that the measured solubility value of 7.8 ug/L indicates that there is some (albeit poor) solubility and consequently long term testing is appropriate for this substance. ECHA concludes that that given the poor solubility of the substance the available short term tests are unreliable and the absence of toxicity in these short term tests is irrelevant. As there are no reliable short-term studies available on aquatic invertebrates or on fish for the registered substance, the integrated testing strategy (ITS) outlined in ECHA *Guidance on information requirements and chemical safety assessment*

(version 4.0, June 2017), Chapter R7b (Section R.7.8.5 including Figure R.7.8-4) is not applicable in this case and long-term studies on both invertebrates and fish are required.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) fish early-life stage (FELS) toxicity test (test method OECD TG 210), fish short-term toxicity test on embryo and sac-fry stages (test method EU C.15. / OECD TG 212) and fish juvenile growth test (test method EU C.14. / OECD TG 215) are the preferred tests to cover the standard information requirement of Annex IX, Section 9.1.6.

However, the FELS toxicity test according to OECD TG 210 is more sensitive than the fish, short-term toxicity test on embryo and sac-fry stages (test method EU C.15 / OECD TG 212), or the fish, juvenile growth test (test method EU C.14. / OECD TG 215), as it covers several life stages of the fish from the newly fertilized egg, through hatch to early stages of growth (see ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), *Chapter R7b, Figure R.7.8-4).*

Moreover, the FELS toxicity test is preferable for examining the potential toxic effects of substances which are expected to cause effects over a longer exposure period, or which require a longer exposure period of time to reach steady state (ECHA *Guidance Chapter R7b,* version 4.0, June 2017).

Your comments on this request were similar to those under section 4 above. You further highlighted that the current request involves testing vertebrate animals. ECHA accordingly refers to ECHA's reply in section 4 above.

A Member State Competent Authority (MSCA) submitted a Proposal for Amendment (PfA) questioning the need for chronic fish study based on the low solubility of the substance as obtained from the OECD TG 105 water solubility study. The PfA also notes that if ECHA considers the solubility of the registered substance such that chronic testing is required, the Registrant should be given the possibility to apply the aquatic ITS given in ECHA guidance R.7.b whereby only the chronic daphnia study and refinement of risk assessment could be sufficient. In your comments on the PfA you agree with the MSCA and indicate that if seen necessary by ECHA you will carry out the chronic Daphnia study and consider the need for chronic fish testing based on the results of the Daphnia study and the transformation dissolution study you intend to carry out. However, ECHA notes that currently neither transformation dissolution data nor chronic aquatic data on invertebrates and fish is available and ECHA considers chronic aquatic testing necessary as discussed below.

While the PfA considers the results of the OECD TG 105 study ECHA notes as the substance is inorganic, information derived from a transformation dissolution study (OECD GD 29) would be more relevant in assessing the availability of the substance to aquatic organisms. This is also the approach brought forward by you in your comments on the DD and PfA. ECHA notes also that in the acute daphnia study available in the technical dossier analytical monitoring took place and the mean measured neodymium concentration was 0.26 mg/L

(0.55 mg/L at start, 0.13 mg/L at the end), also implying that the low solubility obtained in the OECD TG 105 study may not be the best measure of the availability of neodymium.

ECHA also disagrees that in this case it would be possible to adapt the long-term fish testing and that only the long-term daphnia study may be required. Section R.7.8.5.3 Conclusions on Chemical Safety Assessment (PNEC Derivation) describes the possibilities for the prediction of relative species sensitivities. It is described that a long-term toxicity study on fish is needed if fish are likely to be more sensitive than invertebrates and algae or the relative sensitivity of fish cannot be predicted. The latter is true for this substance which has low water solubility and there was no effects in short-term studies which could have been used to indicate relative species sensitivity. In addition in the ITS Step 6 in the abovementioned section of ECHA Guidance "Intrinsic physico-chemical properties", it is outlined that for poorly water soluble substances it should instead of an acute test be considered to perform a long term test (REACH Annex VII and VIII, 9.1).

In summary, as described above the available data indicates that while the substance can be considered poorly soluble its solubility and availability is not such that chronic aquatic testing could be waived. As explained above, ECHA also considers that the aquatic toxicity potential of poorly soluble substances can only be accurately assessed with long-term data and for the purpose of Chemical Safety Assessment and PNEC derivation chronic testing of three trophic levels, invertebrates, algae and fish, is required.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit information generated with a test material representative of the registered substance subject to the present decision: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

Notes for your consideration

Once results of the test on long-term toxicity to fish are available, you shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation.

Due to the low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

6. Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Activated sludge respiration inhibition testing" is a standard information requirement as laid down in Annex VIII, Section 9.1.4. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of an activated sludge respiration inhibition in the dossier that would meet the information requirement of Annex VIII, Section 9.1.4.

You have sought to adapt this information requirement according to Annex VIII, Section 9.1.4., column 2. You provided the following justification for the adaptation "*In accordance with the column 2 adaptation of REACH Annex VIII, the activated sludge respiration inhibition study (required in section 9.1.4) does not need to be conducted as the substance is highly insoluble in water.*"

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex VIII, Section 9.1.4., column 2 because ECHA considers that "*mitigating factors indicating that microbial toxicity is unlikely to occur, for instance the substance is highly insoluble in water*" are not demonstrated. You claim that the substance is highly insoluble but ECHA notes that the measured solubility value of 7.8 ug/L indicates that there is some (albeit poor) solubility and consequently your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) activated sludge respiration inhibition test (carbon and ammonium oxidation) (test method OECD TG 209) is the preferred test to cover the standard information requirement of Annex VIII, Section 9.1.4.

In your comments on the draft decision, you noted that the REACH Regulation does not specify what is meant by "highly insoluble" as mentioned in the specific rules for adaptation of Annex VIII, Section 9.1.4., column 2. In the absence of a clear definition of "highly insoluble" substances, you referred to the water solubility classification as mentioned in the EPI Suite™-Estimation Program Interface from US EPA. Based on this classification, you stated that neodymium oxide should be considered to have negligible solubility (i.e. water solubility below 0.1 mg/L). Based on the above, you consider that your adaptation is valid unless ECHA can provide with a lower cut-off value. In such a case, you would reconsider the water solubility profile of the substance.

ECHA emphasises that for aquatic toxicity testing (Section 9.1 of Annexes VII and VIII), Column 2 refers to mitigating factors indicating that aquatic toxicity is unlikely to occur. In this context, a general threshold for the concept of "highly insoluble in water" cannot be established as it depends on the intrinsic properties of each individual substance as explained in ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7b: Endpoint specific guidance (Version 4.0, June 2017). Accordingly, the waiving statement should not simply refer to a given water solubility classification scheme but should aim at justifying that aquatic solubility is unlikely to occur at the water solubility limit. If registrants cannot demonstrate that aquatic toxicity is unlikely to occur, the substance should be considered as "poorly water soluble", not as "highly insoluble in water".

ECHA notes that you did not demonstrate that toxicity towards aquatic micro-organisms is unlikely. In addition, you did not demonstrate that the test could not be conducted for technical reasons (as per Annex XI, Section 2). Accordingly, the information gap remains and you need to generate information to address this.

ECHA notes further that in your comments on the DD for the endpoints relating to long-term aquatic toxicity testing you indicated that "*conducting ecotoxicity studies on the metal itself or a poorly soluble metal compound is of limited value due to difficulties related to the dissolution of the test substance*", hence the soluble ion should be tested instead. The approach for testing described in ECHA's reply to your comments in request 4. is also applicable here and testing the soluble ion instead of the registered substance would appropriately assess the toxicity of the registered substance.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with a test material representative of the registered substance subject to the present decision: Activated sludge, respiration inhibition test (carbon and ammonium oxidation) (test method: OECD TG 209).

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 18 September 2017.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

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

ECHA took into account your comments and amended the requests.

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

ECHA received proposal(s) for amendment and did not modify the draft decision.

ECHA invited you to comment on the proposed amendment(s).

ECHA referred the draft decision to the Member State Committee.

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

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-61 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

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

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants. Based on the information reported in IUCLID section 1.2 *"Hexagonal and cubic structural forms of the substance may exist and these are both covered by the boundary composition."*

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades (e.g. hexagonal and cubic forms), the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.