Helsinki, 25 July 2019

Addressee: [redacted]

Decision number: CCH-D-2114476155-46-01/F
Substance name: Blue sodium polysulfide aluminosilicate with a SOD-type framework structure
EC number: not applicable*, previously 309-928-3
CAS number: N/A
Registration number: [redacted]
Submission number: [redacted]
Submission date: 26/03/2014
Registered tonnage band: Over 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. **Water solubility (Annex VII, Section 7.7.; test method: EU A.6./OECD TG 105) with the registered substance;**

2. **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;**

3. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) in a second species (rat or rabbit), oral route with the registered substance;**[1]

4. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route with the registered substance specified as follows:**
   - **Ten weeks premating exposure duration for the parental (P0) generation;**
   - **Dose level setting shall aim to induce systemic toxicity at the highest dose level;**
   - **Cohort 1A (Reproductive toxicity);**
   - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;**

* The technical dossier contains the following disclaimer in section 1.1: "*This EC entry is not appropriate to identify the registered substance. This identifier cannot be modified in the present registration at this stage for technical reasons*". In addition, the registrant has provided the IUPAC name "Blue sodium polysulfide aluminosilicate with a SOD-type framework structure". Therefore, this decision refers to the substance as identified by its IUPAC name, and not by EC inventory number.

5. **Robust study summary for key study [redacted], Growth inhibition study aquatic plants (Annex VII, Section 9.1.2. in conjunction with Annex I, Section 3.1.5);**

   or

   Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: Alga, growth inhibition test, EU C.3./OECD TG 201) with the registered substance;

6. **Robust study summary for key study [redacted], Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5. in conjunction with Annex I, Section 3.1.5);**

   or

   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 the registered substance;

7. **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 the registered substance;**

You are required to submit the requested information in an updated registration dossier by ***1 February 2022***. You shall also 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[2] by Ofelia Bercaru, Head of Unit, Hazard Assessment

[2] 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

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation.

1. Water solubility (Annex VII, Section 7.7.)

"Water solubility" is a standard information requirement as laid down in Annex VII, Section 7.7 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 provided the results of a water solubility study according to OECD 105/EU A.6 test guideline using the column elution method. You report a water solubility value of 1.1-1.3 mg/L at 20 °C and pH 6.8. You report the selection of the method to be based on a preliminary water solubility test without providing any raw data from the preliminary test. In addition, you justify the selection of column elution method with water solubility being < 0.01 g/L in the preliminary test.

According to ECHA Guidance R.7a[3] a column elution method is suitable for essentially pure organic substances. The registered substance is an inorganic UVCB and therefore, the column elution method is not an appropriate choice to determine the water solubility for this type of substances. The results reported by you cannot therefore be considered reliable.

Regarding the sensitivity of the test method, other test methods can be used to detect water solubility below 0.01 g/L (e.g. ECHA Guidance R.7a mentions that the flask method can measure water solubilities down to 1 µg/L).

In your comments to the draft decision you indicated that you are willing to perform a new water solubility study according to the flask method, although the EU A.6 test guideline recommends the column elution method for substances with low solubility (<0.01 g/l). ECHA highlights that the flask method is more suitable for mixtures (as the registered substance is) and can also be applied to low solubility substances, provided that slow-stirring technique is used, as explained in the ECHA Guidance R.7a.

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.

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: Water solubility (test method: OECD TG 105).

Guidance for determining appropriate test methods for the water solubility is available in the ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017), Chapter R.7a, Section R.7.1.7.

[3] Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a: Endpoint specific guidance, Version 6.0, July 2017

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

A "Pre-natal developmental toxicity study" (test method 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.
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) with the registered substance.

However, the OECD TG 422 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.

In your IUCLID dossier, you have also provided one non-guideline, no GLP compliant developmental study, performed with the registered substance, administered in the diet for only 7 days before mating ([redacted] *1966*). You have assigned a reliability score of 3 (not reliable), due to "*significant methodological deficiencies. The study is not well documented*".

ECHA agrees that this study is not reliable, and it also does not cover key parameters of a pre-natal developmental toxicity study. Therefore, it does not provide the information required by Annex IX, Section 8.7.2.

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 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 powder, ECHA concludes that testing should be performed by the oral route.

In your comments to the draft decision you consider that "*animal testing for this endpoint is not justified*". Firstly, you refer to the OECD TG 414 guideline in its part describing the selection of the doses. You conclude that "*Testing at a higher dose than the limit test (1000 mg/kg-bw) would be senseless in terms of animal welfare and regarding human risk assessment*". ECHA points out that it is at your own discretion to perform the test with three dose levels or a limit test. If the requirements for the limit test are met, there is no need to perform the test with doses higher than 1000 mg/kg bw/day.

Secondly, you claim that the available sub-acute and sub-chronic data showed effects "*related to the physical erosion induced by the silica at high doses which are not relevant for human risk assessment*" and further that "*No effects are foreseen for the reproductive and development endpoints*".

As explained in the draft decision sent to you, those studies do not cover key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations.

ECHA reiterates that a pre-natal developmental toxicity study is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation.

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.

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

Pre-natal developmental toxicity studies (test method OECD TG 414) on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

There is no information provided for a pre-natal developmental toxicity study in a second species. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with rabbits or rats as a second species, depending on the species tested in the first pre-natal developmental toxicity study.

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 powder, ECHA concludes that testing should be performed by the oral route

In your comments to the draft decision you state that "*This assay is not intended as a first-tier approach, but just justified when clear alerts appear on the reproductive/development impairment by the chemical, what is not the case, as explained in the point above (8.7.2)".*

As explained in the draft decision sent to you, a pre-natal developmental toxicity study in the second species is a standard information requirement for substances registered at 1000 tonnes or more unless the specific rules for adaptation in Annex X, Section 8.7., column 2 or the general rules for adaptation in Annex XI are met.

ECHA notes that your statement is not based on any adaptation possibilities and you did not provide any scientific justification in accordance with the appropriate rules in the respective annexes, supported with an adequate and reliable documentation.

Further, ECHA points out that the information requirements in column 1 of section 8.7.2. at Annex X is cumulative to Annex IX, section 8.7.2., requiring one prenatal developmental

toxicity study more in addition to that required in Annex IX. Thus, at Annex X level information on two species is required.

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 second species (rabbit or rat) by the oral route.

Notes for your consideration

You are reminded that before performing a pre-natal developmental toxicity study in a second species you must consider the specific adaptation possibilities of Annex X, Section 8.7., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species with other available information enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement.

4. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

The basic test design of an extended one-generation reproductive toxicity study (test method OECD TG 443 with Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of 8.7.3., Annex X. If the conditions described in column 2 of Annex X are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3. Further detailed guidance on study design and triggers is provided in the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).

Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

a) The information provided

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 X, Section 8.7.3. because it does not cover key elements, such as exposure duration, life stages and statistical power of an extended one-generation reproductive toxicity study. More specifically, the main missing key elements are: 10 weeks pre-mating exposure duration, at least 20 pregnant females per group, and an extensive postnatal evaluation of the F1 generation.

Moreover, you provided the following justification for an adaptation of the required information: "*In accordance with column 2 of REACH Annex IX, the two-generation reproductive toxicity study (required in section 8.7.3) does not need to be conducted as the 28-day and 90-day study results do not indicate adverse effects on reproductive organs or tissues*".

However, ECHA notes that the substance is registered for a tonnage band of more than 1000 tonnes per year and that you therefore are also obliged to provide the information

specified in Annex X to the REACH Regulation. Different from the information requirements under Annex IX, which you refer to, the information requirement under Annex X, Section 8.7.3 is not dependent on indications of adverse effects on reproductive organs or tissues from available repeated dose toxicity studies.

b) The specifications for the study design

Premating exposure duration and dose-level setting

To ensure that the study design adequately addresses the fertility endpoint, the duration of the premating exposure period and the selection of the highest dose level are key aspects to be considered. According to ECHA Guidance, the starting point for deciding on the length of premating exposure period should be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).

The highest dose level shall aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

If there is no relevant data to be used for dose level setting, it is recommended that results from a range-finding study (or range finding studies) are reported with the main study. This will support the justifications of the dose level selections and interpretation of the results.

Species and route selection

According to the test method OECD TG 443, the rat is the preferred species. On the basis of this default assumption, ECHA considers that testing should be performed in rats.

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 powder, ECHA concludes that testing should be performed by the oral route.

In your comments to the draft decision you argue that the extended-one generation toxicity study is not justified "*According to column 1 point 8.7.3 states that Extended one-generation reproductive study (…) should be carried out if the available repeated dose toxicity studies (e.g. 28-days or 90-days studies, OECD 421 or 422 screening studies) indicate adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity*".

ECHA notes that your justification is based on a wrong legal reference; i.e. Annex IX, Section 8.7.3 column 1 of the REACH Regulation. You have registered your substance for 1000 tonnes

or more per year. ECHA reiterates that the extended one-generation reproductive toxicity study (OECD TG 443) is a standard information requirement at REACH Annex X, Section 8.7.3.

c) Outcome

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: Extended one-generation reproductive toxicity study (test method OECD TG 443), in rats, oral route, according to the following study-design specifications:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce systemic toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;

While the specifications for the study design are given above, you shall also submit with the new endpoint study record a scientific justification on each of the following aspects: 1) length of the premating exposure duration and dose level selection, 2) reasons for why or why not Cohort 1B was extended, 3) termination time for F2 generation, and 4) reasons for why or why not Cohorts 2A/2B and/or Cohort 3 were included.

Notes for your consideration

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3, if new information becomes available after this decision is issued to justify such an inclusion. Inclusion is justified, if the available information, together with the new information shows triggers which are described in column 2 of Section 8.7.3., Annex X and further elaborated in ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017). You may also expand the study to address a concern identified during the conduct of the extended one-generation reproduction toxicity study and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the expansion must be documented.

5. **Robust study summary for key study [redacted], Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.);**

   OR

   Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: Algae, growth inhibition test, EU C.3./OECD TG 201) with the registered substance

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. 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.

Pursuant to Articles 10(a)(vii) of the REACH Regulation, the information set out in Annexes VII to XI must be provided in the form of a robust study summary, if required under Annex I. Article 3(28) of the REACH Regulation defines a robust study summary as a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report. Guidance on the preparation of the robust study summaries is provided in the ECHA Practical Guide 3: 'How to report robust study summaries'.

Furthermore, pursuant to Article 10(a)(vii) and Annex I, Section 3.1.5. where there is more than one study addressing the same effect, then the study or studies giving rise to the highest concern shall be used to draw a conclusion and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust study summaries will be required of all key data used in the hazard assessment.

In the technical dossier you have provided the following study record to fulfil the standard information requirement of Annex VII, Section 9.1.2.: Key study, reliability 1, [redacted] GLP compliant, OECD Guideline 201 (Alga, Growth Inhibition Test).

However, you have not provided sufficient information in the technical dossier to allow the assessment of the reliability of this key study.

In particular, ECHA considers that as neither nominal nor measured test concentrations nor information on test solution preparation is reported the actual exposure concentrations are unknown. You have indicated that analytical monitoring took place, however in terms of information on test concentrations, and results, you have merely reported that "*The results were as follows: EC50 (72h) >99 mg/L NOEC (72h) >99 mg/L*" (based on growth rate). Your substance is marketed as a solid (powder) and its water solubility is questionable (please refer to request 1.). However, based on the information provided the water solubility can be assumed to be low. Due to its properties your substance is likely difficult to test in aqueous media. For such substances information on test solution preparation and analysis of test concentration is particularly important to be able to confirm exposure.

In absence of information on test concentrations (nominal and measured) and test solution preparation it is not possible for ECHA to assess whether the result of "*> 99mg/L*" is representative of the exposure and whether the requirement of paragraph 39 of the OECD TG 201 of test concentrations being maintained within 20 % of the nominal throughout the test has been fulfilled. Lastly, in some of the other aquatic studies (please see below) included in your technical dossier decantation of the test material was reported which further highlights that quantification of exposure concentrations and information on test solution preparation is essential to be able to assess the validity of the study.

Furthermore, while ECHA acknowledges that you have indicated that validity criteria were fulfilled in the study no information on biomass and on growth rates in the control cultures during the test is given. Thus, it is not possible for ECHA to verify whether the validity criteria as specified in the OECD TGD 201, paragraph 11, were met.

Based on the above, ECHA notes that, contrary to Article 3(28) of the REACH Regulation the documentation of the key study is insufficient and does not allow an independent assessment of the adequacy of the study, their results and use for hazard assessment. ECHA refers you to ECHA Practical Guide 3: 'How to report robust study summaries' (version 2.0 November 2012) for a comprehensive list of the elements that should be reported in the RSS of an Algal growth inhibition test (page 47).

ECHA notes that in addition to the key study you have submitted [redacted] conducted according to guideline "NF T90-375 /NF EN 28692" as a supporting study for this endpoint. You have indicated that the study is reliability 4, non GLP and that it is not well documented. The results have been reported only as "*EC50 (72h) = 0.54% (test material decanted 2 hours), 22.5% <EC50 (72h) < 90% (test material decanted 2 hours + centrifugated).*" You have also indicated that "*There is no data about the concentration of the test material.*" ECHA agrees that the study is not reliable and cannot be used to conclude on this endpoint, most importantly due to lack of information on test concentrations and numerical effect values, exact guideline and its validity criteria and information on controls.

Hence, 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, as defined below.

In your comments to the draft decision, you agree to update the robust study summary and indicate that you will contact [redacted] to obtain information on the preparation of the test solutions.

Furthermore, while you acknowledge that the substance is difficult to test in water due to its low water solubility, you consider that it is obvious that the test substance will be present at its maximum solubility in the aquatic media and that information on the exposure concentration is only relevant in tests where effects are observed. As explained in the draft decision sent to you, due the substance properties, exposure to the test substance cannot be confirmed in the absence of information on test solution preparation and analysis of test concentration. ECHA points out that, since no effects were observed in this study, confirmation that exposure took place is important in order to assess the reliability of the results of this study.

Finally, regarding the reliability of the study, you further point out the relevance of the internationally recognised institute that performed the study. However, with the information currently available on the study ECHA cannot evaluate the adequacy of a study.

In order to allow an independent assessment of the key study submitted, pursuant to Article 41(1) and (3) of the REACH Regulation you are requested to provide a complete robust study summary with the missing elements identified above for the key study.

Alternatively, if you cannot submit a complete RSS for the key study or the RSS indicates that the key study is not reliable as per the criteria indicated above and/or not adequate to fulfil the information requirement, 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: Algae growth inhibition test, EU C.3./OECD TG 201.

6. **Robust study summary for key study [redacted] (Annex IX, Section 9.1.5. in conjunction with Annex I, Section 3.1.5);**

   OR

   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 the registered substance;

"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.

In the technical dossier you have submitted the following adaptation according to Annex IX, Section 9.1.5., column 2: "*In accordance with column 2 of REACH Annex IX, the long-term toxicity testing on invertebrates (required in section 9.1.5) does not need to be conducted as the chemical safety assessment indicates no need to investigate further the effects on aquatic organisms*".

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.5., column 2 because of the following.

While the water solubility of your substance is questionable (please refer to request 1.), based on the information provided and due to substance properties the water solubility can be assumed to be low and long-term testing is indicated as discussed in the following.

Poorly soluble substances require longer time to be taken up by test organisms and therefore steady-state conditions are likely not reached within the duration of a short-term toxicity test. For this reason, short-term tests may not give a true measure of toxicity for poorly soluble substances and toxicity may actually not even occur at the water solubility limit of the substance during an acute study of short duration. ECHA notes that this is true for your substance as in the acute studies on fish and daphnids included in your dossier no effects were observed whereas in the long-term daphnia study (addressed below) effects were seen.

ECHA hence considers that it is not possible to derive a reliable PNEC for a poorly water soluble substance with acute data alone, particularly when no effects are observed in acute studies. For the derivation of PNECaquatic reliable information on three trophic levels is required. With the inadequacies in reporting in the available aquatic plants (request 5 above) and long-term daphnia studies (as addressed below) and in absence of information on long-term toxicity to fish you currently have no reliable long-term data available to enable you to derive a reliable PNEC and to carry out a risk assessment.

Information on long-term toxicity testing on aquatic organisms shall also be considered for the classification and labelling of the substance. Hence if toxicity is observed in these studies, the classification of the substance might have to be revised. Therefore, as the hazard and risk assessments provided in your dossier are not conclusive, ECHA considers that the available information in your chemical safety assessment does not rule out the need to investigate long-term effects to aquatic invertebrates.

In addition to the adaptation addressed above, in the technical dossier you have also provided the following study record to fulfil the standard information requirement of Annex IX, Section 9.1.5.: Key study, reliability 1, [redacted], GLP compliant, OECD Guideline 211 (Alga, Daphnia magna Reproduction Test).

Pursuant to Article 10(a)(vii) of the REACH Regulation, the information set out in Annexes VII to XI must be provided in the form of a robust study summary, if required under Annex I. Article 3(28) of the REACH Regulation defines a robust study summary as a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report. Guidance on the preparation of the robust study summaries is provided in the Practical Guide 3 "How to report robust study summaries".

Furthermore, pursuant to Article 10 (a)(vii) and Annex I, Section 3.1.5. of the REACH Regulation if there are several studies addressing the same effect, then, the study or studies giving rise to the highest concern shall be used to draw the conclusion and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust study summaries will be required of all key data used in the hazard assessment.

ECHA notes that regarding the key study you have not provided sufficient information in the technical dossier to allow assessment of reliability of the study.

In particular, ECHA considers that as neither nominal nor measured test concentrations nor information on test solution preparation is reported the actual exposure concentrations are unknown. You have indicated that analytical monitoring took place, however in terms of information on test concentrations you have merely reported the effect values "*EC50 (21d) =34 mg/L, NOEC (21d) =26 mg/L*". As already discussed above in request 5. due to its properties, information on test concentrations (nominal and measured) and test solution preparation are needed to allow assessment of the reliability of the study and of whether the effect value provided reflect the actual exposure of the tests organisms. It is also not possible to assess whether the requirement of paragraph 48 of the OECD TG 211 of test concentrations being maintained within 20 % of the nominal throughout the test has been fulfilled.

Furthermore, while ECHA acknowledges that you have indicated that validity criteria were fulfilled in the study, no information on the test organisms and the control organisms is provided. Hence it is not possible to assess whether the validity criteria specified in the OECD TGD 211, paragraph 8, relating to mortality of parent organisms and mean number of live offspring produced per parent, were met.

Furthermore, other important information, such as details on the test organisms (e.g. age at initiation of test), test conditions such as pH, oxygen and temperature, has not been given in the RSS. In absence of such information ECHA cannot evaluate whether the test was reliably performed according to OECD TG 211.

ECHA notes that, contrary to Article 3(28) of the REACH Regulation the documentation of the study is insufficient and does not allow an independent assessment of the adequacy of the study, their results and use for hazard assessment. ECHA refers you to ECHA Practical Guide 3: 'How to report robust study summaries' (version 2.0 November 2012) for a comprehensive list of the elements that should be reported in the RSS of Long-term toxicity on aquatic invertebrates test (page 46).

In summary, as the adaptation submitted for this endpoint in the technical dossier is not acceptable and the information provided on the key study submitted does not allow to assess its reliability, 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, as defined below.

In your comments to the draft decision, you agree to update the robust study summary and indicate that you will contact [redacted] to obtain further unpublished information. Regarding the reliability of the key study, you state that the study was performed by an internationally recognised authority. However, as indicated above and already in the initial draft decision, with the information currently available on the study ECHA cannot evaluate the adequacy of a study.

You agree with ECHA's rejection of the adaptation according to Annex IX, Section 9.1.5 column 2., and indicate that you will remove the adaptation from your technical dossier.

In order to allow an independent assessment of the key study submitted, pursuant to Article 41(1) and (3) of the REACH Regulation you are requested to provide a complete robust study summary with the above missing elements for the key study.

Alternatively, if you cannot submit a complete RSS or the RSS indicates that the study is not reliable and not adequate to fulfil the information requirement, 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: Daphnia magna reproduction test (test method: EU C.20./OECD TG 211).

7. 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 the registered substance;

"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 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 of REACH Annex IX, the long-term toxicity testing on fish (required in section 9.1.6) does not need to be conducted as the chemical safety assessment indicates no need to investigate further the effects on aquatic organisms.*"

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.6., column 2. As already fully discussed in the statement of reasons under point 6 above, the hazard and risk assessments provided in your dossier are not conclusive and therefore the available information in your chemical safety assessment does not rule out the need to investigate long-term effects to aquatic organisms, here fish.

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) can be performed 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, Section R.7.8.4.1.*

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).

In your comments to the draft decision, you do not agree to conduct the study requested. You indicate that animal testing should be the last resort and you propose to provide further information on the behaviour and stability of the substance at different pH, as well as on its molecular size. ECHA understand that you propose to adapt the current information requirement based on your claim that the substance is expected to have low to null bioavailability to fish.

ECHA points out that long-term toxicity testing on fish is a standard information requirement for substances registered at 1000 tonnes or more unless the specific rules for adaptation in Annex IX, Section 9.1., column 2 or the general rules for adaptation in Annex XI are met.

ECHA notes that your claim is not based on any adaptation possibilities and you did not provide any scientific justification in accordance with the appropriate rules in the respective annexes, supported with an adequate and reliable documentation.

In particular, regarding your claim that the substance is expected to have low to null bioavailability to fish, ECHA notes that this is not an acceptable adaptation for the following reasons. Firstly, while column 2 of REACH Annexes VII and VIII contains the provision that acute studies do not need to be conducted if there are mitigating factors indicating that aquatic toxicity is unlikely to occur (e.g. if the substance is highly insoluble in water or is unlikely to cross biological membranes), REACH asks registrant to consider long-term studies when a substance is poorly water soluble, as in your case. Secondly, your claim that the substance is expected to have low to null bioavailability is not substantiated by any scientific evidence but is merely based on low solubility, stability at different pH and molecular mass around 900-1000. However, ECHA points out that there is no scientific basis to define a cut off limit value for solubility below which no toxicity could occur, nor to define molecular characteristics that would render a substance unlikely to cross biological membranes, as explained in Section R.7.8.5 of ECHA Guidance Chapter R.7b (version 4.0, June 2017). Finally, ECHA notes that effects have been observed in the long-term daphnia study (*"EC50 (21d) =34 mg/L, NOEC (21d) =26 mg/L"*, study addressed in point 6. above). While the full reliability of the study cannot be assessed due to poor reporting, the results indicate that the substance is bioavailable to aquatic organisms. You have not provided any scientific explanation as to why the substance would be bioavailable to aquatic invertebrates but not to fish.

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: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

Notes for your consideration for requests 5 to 7

Once results of the aquatic tests requested above are available, you shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation.

ECHA notes that due to lack of effects in short-term studies it is not possible to determine the sensitivity of species. Therefore, 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 the long-term studies on both invertebrates and fish are requested to be conducted.

Due to the properties of the substance (e.g. low solubility, colour) 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).

Consideration on uses of the substance in relation to the tests requested in the decision

In your comments to the draft decision you discuss that the substance has several different uses, such as [redacted] and uses in the [redacted]. You state that as those uses fall under Article 14. 5 (a) and (b) of the REACH Regulation, no risk

assessment for those is required. You further argue that "*This should be considered for the standard information requirements adaptation*" under Annex XI, section 3.

ECHA agrees that for the uses [redacted] and [redacted] risk assessment evaluation is not needed. However, as you also state in the comments "*the substance is intended for several different uses*". In the Chemical Safety Report (CSR) and in the technical dossier you reported uses such as: biocidal products (e.g. disinfectants, pest control), coatings and paints, thinners, paint removes, washing and cleaning products (including solvent based products) etc., which are out of the scope of Article 14. 5(a) and (b).

As stated in Annex XI, Section 3, you may adapt the information requirement, provided you fulfil all the identified criteria in paragraphs 3.2(a)(i) to (iii) and submit an adequate and scientifically-supported justification, based on a thorough and rigorous exposure assessment in accordance with Section 5 of Annex I.

You did not provide quantitative exposure assessment for uses described above, and did not calculate the Risk Characterisation Ratios (RCRs). Therefore, the adaptation requirements of Annex XI, section 3 are not met.

In your comments to the draft decision you also claim that as the substance is intended for the cosmetic sector, no animal testing should be performed since "*otherwise, according to the Cosmetics Regulation (EC) N° 1223/2009, the substance cannot be used for this purpose*". You argue that "*this is not in line with ECHA's directions regarding the coexistence of both regulations*".

ECHA points out that according to the ECHA factsheet available on the interface between REACH and Cosmetics Regulations, which was developed jointly with the European Commission[1], the Cosmetics Regulation does not restrict testing under REACH, if this testing is required for environmental endpoints or the substance is also registered for non-cosmetic uses. As explained above, in the CSR you have reported many product categories/market uses for the registered substance. Furthermore, even if a substance is registered exclusively for cosmetic use, the animal testing requirements continue to apply to tests needed to assess the risks from exposure to workers in the Chemical Safety Assessment. Such testing would not trigger the testing and marketing bans under the Cosmetics Regulation as the testing is to be performed for the purposes of meeting the requirements of the REACH Regulation; see Commission Communication of 11 March 2013 on the animal testing and marketing ban and on the state of play in relation to alternative methods in the field of cosmetics (COM(2013)135)).

Further information is available at https://www.echa.europa.eu/-/clarity-on-interface-between-reach-and-the-cosmetics-regulation.

[1] Please see https://echa.europa.eu/documents/10162/13628/reach_cosmetics_factsheet_en.pdf

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 30 May 2018.

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, including your request for an extension of the commenting period on the draft decision. ECHA did not amend the request(s).

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

As no amendments were proposed, ECHA took the decision according to Article 51(3) 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.

   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, 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.