Helsinki, 8 September 2016

Addressee: [redacted]

Decision number: CCH-D-2114340955-43-01/F
Substance name: diammonium peroxodisulphate
EC number: 231-786-5
CAS number: 7727-54-0
Registration number: [redacted]
Submission number: [redacted]
Submission date: 01.10.2010
Registered tonnage band: 1000+T

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);**

2. **Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1; test method: EU C.7/OECD TG 111) with the registered substance;**

3. **In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, EU B.13/14 /OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102 using the registered substance;**

4. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2; test method: EU B.31/OECD TG 414) in a first species (rats or rabbits), oral route with the registered substance;**

5. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2; test method: EU B.31/OECD TG 414) in a second species (rats or rabbits), oral route with the registered substance;**

6. **Extended one-generation reproductive toxicity study (test method EU B.56/ OECD TG 443), in rats, oral route, with the registered substance according to the following study-design specifications:**
   - **Ten weeks premating exposure duration for the parental (P0) generation;**
   - **Dose level setting shall aim to induce some 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**

7. **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;**

8. **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;**

9. **Identification of DNELs and risk characterisation (Annex I, Sections 1.4. and 6.): Revise acute and long-term DNEL(s) for workers inhalation and dermal routes local effects using the default assessment factors and other recommendations of ECHA Guidance R.8 for DNEL derivation and revise the risk characterisation accordingly *or* provide a detailed justification for not using the recommendations of ECHA Guidance R.8 for DNEL derivation;**

10. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health: provide a qualitative exposure assessment demonstrating the likelihood that effects of inhalation and skin sensitisation are avoided for all worker and consumer exposure scenarios and detail the operational conditions and risk management measures and revise the exposure assessment and risk characterisation accordingly;**

11. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: revise the environmental exposure estimation and risk characterisation.**

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 of the REACH Regulation. In order 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 an adequate and reliable documentation. In this respect ECHA refers you to Appendix 3 of the present decision. There you are invited to consider which substance(s) within the category to use for testing in order to apply a grouping of substances and read across approach within the category to fulfil the missing information requirements.

Deadline for submitting the required information

Pursuant to Articles 41(4) and 22(2) of the REACH Regulation, you shall submit to ECHA an update of the registration dossier containing the information specified under item 10 in this decision by **15 March 2017**.

Pursuant to Articles 41(4) and 22(2) of the REACH Regulation, you shall submit to ECHA an update of the registration dossier containing the information specified under items 1 to 9 and 11 in this decision by **15 September 2020**. You shall also update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

Note for information to the Registrant

In this specific case, considering the skin and respiratory sensitising properties of the substance, two deadlines are set in this decision in order to ensure adequate protection of the health of workers and consumers without undue delay, while still allowing sufficient time for conducting new tests.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. 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, shall 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 Ofelia Bercaru, Head of Unit, Evaluation E3

[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

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

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

Annex VI, section 2.3.7 of the REACH Regulation requires that each registration dossier contains a sufficiently detailed description of the analytical method used for establishing the composition of the registered substance and therefore its identity. This information shall be sufficient to allow the method to be reproduced.

You have included in section 1.4 of the IUCLID dossier results of 1H-NMR, UV-VIS, FTIR, MS and a semiquantitative XRF analysis for the identification and quantification of the substance.

However, the analytical methods included in section 1.4 of the IUCLID dossier do not allow for unambiguous identification and quantification of the substance. More specifically, the 1H-NMR analysis do not show any detectable substance specific signals whereas the MS analysis allows identification of the NH4-SO3, SO3, SO2, SO, S and NH3 fractions but not the characteristic signals for the molecular ion of peroxydisulfate. The UV-VIS analysis does not show absorption bands due to the absence of chromophores in the substance, which would absorb in UV-VIS spectral range, and the FTIR analysis allows only identifying the signals from N-H, S=O and S-O bonds. Moreover, the XRF analysis identifies and quantifies sulfur in the substance but no results to identify and quantify the ammonium and peroxydisulfate ions have been included in section 1.4 of the IUCLID dossier.

Therefore, ECHA concludes that the description of the analytical methods for the identification of the substance is not sufficient as required under Annex VI section 2.3.7. of the REACH Regulation.

You shall include in section 1.4 of the IUCLID dossier the description of analytical methods and their results, which allow unambiguous quantification and identification of the ammonium and peroxydisulfate ions. As indicated in section 4.2.1.3 of the Guidance on the identification and naming of substances under REACH and CLP (Version: 1.3, February 2014), for inorganic substances the use of X-Ray Diffraction (XRD) is more suitable than spectroscopic methods to confirm their structure as this method provides a fingerprint of a crystalline inorganic substance. As your substance is a crystalline inorganic substance, you shall include in section 1.4 of the IUCLID dossier results of a XRD analysis, including diffractogram, or suitable alternative data that can provide the same information (e.g. a record that enables the characterisation of the atomic structure of the substance, showing for the match of the identified absorption bands or emission wavelengths of a sample of the substance vs. that of a certified standard reference). The methods used for the quantification and identification of the substance shall be described in such detail that they can be reproduced.

In the comments to the draft decision you have agreed with the information requirement in the draft decision by stating the following "*The registrant notes that the analytical standard requirements (1H-NMR, MS, UV-VIS, FTIR) were done to fulfil ECHAs standard requirements. In the past ECHA often requested these studies even if not meaningful for*

inorganic substances e.g. to allow identification of potential organic impurities. Nevertheless, the registrant agrees to conduct an X-Ray Diffraction (XRD) analysis for identification of this inorganic substance".

2. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

"Hydrolysis as a function of pH" is a standard information requirement as laid down in Annex VIII, Section 9.2.2.1 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.

According to the OECD TG 111 (2004) the hydrolyisis test should be conducted at three temperatures in the range of 10-70 ºC and in the three pHs (4,7,9). Also, the hydrolysis rate and hydrolysis product(s) formed in significant amount ($\geq$ 10%) in pH ranges 4-9 should be determined for 25 ºC. Furthermore, according to OECD TG 111 (2004), additional tests at pH values other than 4, 7 and 9 may be required for a hydrolytically unstable test substance. For example, for physiological purposes a test under more acidic conditions (e.g. pH 1.2) may be required employing a single physiologically relevant temperature (37ºC

In your technical dossier you have provided a publicly available study by I.M. Kolthoff and I.K. Miller, published in 1951.The publication entitled: "The Chemistry of Persulfate. I. The Kinetics and Mechanism of the Decomposition of the Persulfate Ion in Aqueous Medium" provides evidence that potassium persulfates decomposes thermally in aqueous solution by two reactions. Furthermore, it provides evidence that decomposition of persulfate involves different reactions based on the pH of the solution. However, the assessments made in this study were limited to a temperature of 50ºC. According to OECD TG 111 (2004) 50ºC is recommended as suitable temperature for preliminary test for 5 days at pH 4, 7, 9, if the test substance is not known to be hydrolytically unstable.). As the hydrolysis test results reported in your technical dossier do not meet the above requirements of the method OECD TG 111 (Hydrolysis as a function of pH), it is not adequate to fulfil the standard information requirements.

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.

In the comments to the draft decision you have agreed with the information requirement in the draft decision by stating the following "*Thus the registrant accepts ECHA's requirement (technical feasibility provided) but requests ECHA to reduce this information requirement to only one substance preferably diammonium peroxodisulphate*". ECHA has addressed your comments regarding "*Category approach for peroxodisulphates*" in the other draft decisions on Sodium peroxodisulfate and Potassium peroxodisulfate.

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: Hydrolysis as a function of pH (test method: EU C.7/OECD TG 111). This shall include identification and quantification of the hydrolysis products, as described in the test guideline.

3. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

An "*In vitro* gene mutation study in bacteria" is a standard information requirement as laid down in Annex VII, Section 8.4.1. 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.

According to Article 13(3) of the REACH Regulation, tests required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods recognised by the Commission or ECHA.

Other tests may be used if the conditions of Annex XI are met. More specifically, Section 1.1.2 of Annex XI provides that existing data on human health properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3) may be used if the following conditions are met:

(1) Adequacy for the purpose of classification and labelling and/or risk assessment;
(2) Adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3);
(3) Exposure duration comparable to or longer than the corresponding test methods referred to in Article 13(3) if exposure duration is a relevant parameter; and
(4) adequate and reliable documentation of the study is provided.

According to paragraph 13 of the current OECD TG 471 test guideline (updated 1997) at least five strains of bacteria should be used. These should include four strains of *S. typhimurium* (TA1535; TA1537 or TA97a or TA97; TA98; and TA100) that have been shown to be reliable and reproducibly responsive between laboratories. These four *S. typhimurium* strains have GC base pairs at the primary reversion site and it is known that they may not detect certain oxidising mutagens, cross-linking agents and hydrazines. Such substances may be detected by E.coli WP2 strains or *S. typhimurium* TA102 which have an AT base pair at the primary reversion site.

You have provided a test performed with the analogue substance disodium peroxodisulfate in the year 1990 according OECD TG 471 and GLP with an assigned reliability score of 1. ECHA considers that a read-across approach with information from the analogue substance disodium peroxodisulfate can be applied for the endpoint under consideration. However ECHA highlights that the scope of the study conducted on the read across substance does not match the scope of the current OECD test guideline 471.

The study performed on the read across substance used five different strains of *S. typhimurium* TA 1535, TA 1537, TA 1538, TA 98 and TA 100. However, since that study test was conducted, significant changes have been made to OECD TG guideline 471 and this means that the study does not meet the current guidelines, nor can it be considered as providing equivalent data according to the criteria in Annex XI, 1.1.2. of the REACH Regulation.

ECHA concludes that a test using *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102 has not been submitted and that the test using one of these is required to conclude on *in vitro* gene mutation in bacteria.

In the comments to the draft decision you have agreed with the information requirement in the draft decision by stating the following "*the registrant agrees with ECHA that a strain is missing covering an AT base pair at the primary reversion site. The registrant is willing to perform an addition bacterial reverse mutation test (test method: EU B.13/14. / OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102 using the registered substance. The registrant notes that he also agrees to perform the requested study with the two other peroxodisulphates of the category (see above) to strengthen the category approach*".

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: Bacterial reverse mutation test (test method: EU B.13/14. / OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

A "pre-natal developmental toxicity study" 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 sought to adapt this information requirement [according to Annex IX, Section 8.7.2., column 2. You provided the following justification for the adaptation:
"The performance of a developmental toxicity/teratogenicity study for substances of the Persulfate Category is scientifically not justified.
In column 2 of REACH Regulation No. 1907/2006, Annex IX, Sect. 8.7., states as follows:
„Reproductive toxicity studies do not need to be conducted if:
- the substance is known to be a genotoxic carcinogen and appropriate risk management measures are implemented, or
- the substance is known to be a germ cell mutagen and appropriate risk management measures are implemented, or
- the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure."

No evidence of developmental toxicity was revealed in a screening test of reproduction/developmental toxicity with diammonium persulfate in rats according to OECD guideline no. 421 (NOAEL for reproduction/developmental toxicity was >= 250 mg/kg/day). Additionally, as deduced in the toxicokinetic assessment, bioaccumulation of substances of the Persulfate Category is very unlikely to occur and 28 and 90 day oral toxicity studies do not imply of relevant toxicological activity. Therefore, it is very unlikely that persulfates would cause adverse developmental toxicity effects.
Conducting such a study is thus scientifically not justified and not in line with animal welfare."

According to Annex IX, Section 8.7., column 2, "*the studies do not need to be conducted if the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentration below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure*". However, ECHA notes that your adaptation does not meet these specific rules for adaptation for the following reasons:

a) ECHA understands that you have referred to the absence of evidence of developmental toxicity in a screening study performed in rats with the registered substance in order to support a claim of low toxicological activity. You also indicated that 28-day repeated dose toxicity studies and 90-day repeated dose toxicity studies conducted via the oral route with the members of the persulfate category, i.e. disodium peroxodisulfate, diammonium peroxodisulfate and dipotassium peroxodisulfate, "*do not imply of relevant toxicological activity*" and conclude that "*it is very unlikely that persulfates would cause adverse developmental toxicity effects*". ECHA acknowledges that no statistically significant and dose-dependent effects were observed in the screening study for reproductive/developmental toxicity conducted with the registered substance via the oral route, up to the highest dose tested, i.e. 250mg/kg/d.

   However, ECHA points out that the study design of the 28-day repeated dose toxicity studies performed via the oral route using the registered substance or dipotassium peroxodisulfate referred to in your waiving argument and which are reported in the technical dossier were conducted in male animals only and lack investigations on parameters such as haematology, clinical chemistry, urinalysis and histopathology. Therefore, the relevance of this data as supporting evidence for an absence of toxicity should be weighed against the limited scope of the investigations performed in these studies.

   ECHA further observes that signs of local toxicity have been observed in a 90-day repeated dose toxicity study conducted via the inhalation route with the registered substance and in a 90-day repeated dose toxicity study conducted via the oral route with the analogue substance disodium peroxodisulfate.

   Furthermore ECHA highlights that the experimental data set available for the members of the persulfate category provided a basis for classification of the three category members, including the registered substance, for acute toxicity via the oral route, for skin and respiratory sensitisation and for local effects on the skin and the eye. This classification indicates that specific hazardous properties have been identified for the three members of the category on the basis of experimental or human data.

   Therefore, ECHA concludes that the specific criteria for adaptation of the information requirement specified in Annex IX, Section 8.7 column 2 referring to the low toxicological activity of the substance is not met.

b) You refer in your waiving argument to the conclusions of the toxicokinetic assessment for this substance suggesting that "*bioaccumulation of substances of the Persulfate Category is very unlikely to occur and 28 and 90 day oral toxicity studies do not imply of relevant toxicological activity*".

ECHA observes that no toxicokinetic data proving the absence of systemic absorption, as required by the provisions of Annex IX, section 8.7 column 2 has been provided. The meaning of your statement relating to "*relevant toxicological activity*" in 28-day and 90-day repeated dose toxicity studies remains unclear.

ECHA notes that the results from the available 90-day oral repeated dose toxicity study performed with the analogue substance disodium peroxodisulfate provided evidence of local toxicity only, in the conditions of this test, with intestinal changes identified as the leading sign of toxicity to establish the NOAEL in that study. Similarly, the signs of toxicity observed in a 90-day inhalation repeated-dose toxicity study conducted with the registered substance indicate local effects in the trachea and bronchi/bronchioles. However, ECHA emphasises that the members of the persulfate category have all been classified as skin and respiratory sensitisers. Positive results have been observed in LLNA tests suggesting that the substances have the potential to cause lymph node proliferation after dermal exposure.

On the basis of all this information, and in the absence of toxicokinetic data proving the absence of systemic absorption, ECHA considers that the condition for adaptation of the information requirement specified in Annex IX, Section 8.7 column 2 referring to the absence of systemic absorption is not met.

c) Annex IX, section 8.7 column 2 further indicates that "*no or no significant human exposure*" should occur to use these provisions to waive further reproductive toxicity testing.

ECHA observes that you have not addressed this aspect in your waiving argument. Further, based on the information provided in the registration dossier, it appears that the members from the persulfate category are used by professionals and consumers in cosmetics, personal care products, as water treatment chemicals suggesting that human exposure to the registered substance occurs. The technical dossier includes in IUCLID section 7.10 case reports of adverse reactions caused by exposure of professionals and consumers to these substances when used as cosmetics or personal care products. Based on this information, ECHA considers that the condition laid down in Annex IX, Section 8.7. column 2 of no or no significant exposure is not fulfilled.

Based on the above, ECHA concludes that the conditions for adaptation of the standard testing regime according to Annex IX, Section 8.7. column 2 are not all met. Therefore, your adaptation of the information requirement cannot be accepted.

In your comments to the draft decision, you refer to the formation of hydrolysis products which are "*well known in human health toxicology and in some cases are also naturally occurring in the human body*". You point out that "*these species are all known not to cause adverse effects on reproduction (fertility and development)*" and intend to strengthen your argument based on upcoming hydrolysis data. ECHA points out that you have not provided scientific information to support your claim that the hydrolysis products of the substance subject to this decision do not cause adverse effects on fertility or development. However, depending on the nature of the information available on these hydrolysis products and its reliability, ECHA recognises that the considerations made by you may potentially be valuable in the developmental of an adaptation of this information requirement according to the general rules for adaptation presented in Annex XI of the REACH Regulation.

ECHA is of the opinion that the information, as currently provided in your comments, does not provide sufficient elements addressing the deficiencies of the adaptation listed in the present decision. Therefore this information does not lead to a modification of the conclusions of the assessment of this adaptation.

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 4.0, July 2015) R.7a, chapter 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.

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: EU B.31./OECD TG 414) in a first species (rats or rabbits) by the oral route.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

Pre-natal developmental toxicity studies 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).

The technical dossier does not contain information on a pre-natal developmental toxicity study with the registered substance. You have sought to adapt this information requirement according to Annex X, Section 8.7.2., column 2. You provided the same justification for the adaptation as for the standard information requirement for a pre-natal developmental toxicity study in a first species (Annex IX, section 8.7.2.) described in section 4 above

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex X, Section 8.7.2., column 2 for the reasons detailed in section 4 above. Therefore, your adaptation of the information requirement cannot be accepted.

In your comments to the draft decision, you refer to the formation of hydrolysis products which are "*well known in human health toxicology and in some cases are also naturally occurring in the human body*". You point out that "*these species are all known not to cause*

adverse effects on reproduction (fertility and development)" and intend to strengthen your argument based on upcoming hydrolysis data. ECHA points out that you have not provided scientific information to support your claim that the hydrolysis products of the substance subject to this decision do not cause adverse effects on fertility or development. However, depending on the nature of the information available on these hydrolysis products and its reliability, ECHA recognises that the considerations made by you may potentially be valuable in the developmental of an adaptation of this information requirement according to the general rules for adaptation presented in Annex XI of the REACH Regulation.

ECHA is of the opinion that the information, as currently provided in your comments, does not provide sufficient elements addressing the deficiencies of the adaptation listed in the present decision. Therefore this information does not lead to a modification of the conclusions of the assessment of this adaptation.

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 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 4.0, July 2015) R.7a, chapter 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.

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: EU B.31./OECD TG 414) in a second species (rabbits or rats) 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 8.7.2., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.
The basic test design of an extended one-generation reproductive toxicity study (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 section 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. 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 requirement

In the technical dossier you have provided a study record for a reproduction/developmental toxicity screening test conducted with the registered substance and provided the following justification: *"Of the Persulfate Category, only diammonium persulfate was tested for oral reproductive/developmental toxicity in a screening test with rats according to OECD guideline no. 421. No test substance related effects were observed in P and F1 generations. A NOAEL value of 250 mg/kg/day for parental toxicity, reproduction parameters and developmental toxicity was determined. As all substances of the Persulfate Category share the same anionic persulfate moiety and similar toxicological properties a read across approach was applied for dipotassium persulfate and disodium persulfate using results obtained with diammonium persulfate."*

In the technical dossier you have provided a study record for a "reproduction/developmental toxicity screening test" (test method: OECD TG 421). This study does not provide the information required by Annex X, Section 8.7.3., because it does not cover key parameters, exposure duration, life stages and statistical power of an extended one-generation reproductive toxicity study. The main missing key aspects/elements are: 10 weeks pre-mating exposure duration, at least 20 pregnant females per group, and an extensive postnatal evaluation of the F1 generation. Thus, adaptation based on Annex XI, 1.1.2 of REACH cannot be accepted.

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. Thus, an extended one-generation reproductive toxicity study according Annex X, Section 8.7.3. is required. The following refers to the specifications of this required study.

In your comments to the draft decision, you consider that the available data on reproductive toxicity are sufficient and conclusive to meet the information requirement of Annex X, section 8.7.3. As pointed out above and in the draft decision issued to you, the information obtained from a reproduction/developmental toxicity screening study performed according to the OECD TG 421 does not provide the information required by Annex X, Section 8.7.3. The design of this study does not cover key parameters, exposure duration, life stages and statistical power of an extended one-generation reproductive toxicity study. The main missing key aspects/elements are: 10 weeks pre-mating exposure duration, at least 20 pregnant females per group, and an extensive postnatal evaluation of the F1 generation. No other source of information addressing the key parameters exposure duration, life stages and statistical power of an extended one-generation reproductive toxicity study has been provided in the technical dossier or in your comments to the draft decision. Therefore ECHA considers that the information provided on this endpoint for the registered substance does not meet the information requirement.

You refer in your comments to the formation of hydrolysis products which are *"well known in human health toxicology and in some cases are also naturally occurring in the human body"*. You point out that *"these species are all known not to cause adverse effects on reproduction (fertility and development)"* and intend to strengthen your argument based on

upcoming hydrolysis data. ECHA points out that you have not provided scientific information to support your claim that the hydrolysis products of the substance subject to this decision do not cause adverse effects on fertility or development. However, depending on the nature of the information available on these hydrolysis products and its reliability, ECHA recognises that the considerations made by you may potentially be valuable in the developmental of an adaptation of this information requirement according to the general rules for adaptation presented in Annex XI of the REACH Regulation.

The standard information requirement of Annex X, section 8.7.3 for an extended one-generation toxicity study can be adapted according to the specific rules for adaptation detailed in Annex X, 8.7 section column 2 or according to the general rules for adaptation of the standard testing regime listed in Annex XI of the REACH Regulation.
ECHA understands that the information that you provided in your comments also refers to the provisions of Annex X, section 8.7 column 2. As detailed in the draft decision issued to you with reference to the information requirement of Annex IX, section 8.7.2, ECHA considers that the criteria of Annex IX and X, section 8.7 column 2 are not all met.
ECHA is of the opinion that the information, as currently provided by you in your comments, does not provide sufficient information addressing the deficiencies of the adaptation listed in the present decision with regard to the provisions of Annex IX and X, section 8.7 column 2. Therefore, this information does not lead to a modification of the conclusions of the assessment of this adaptation.

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 R.7a, chapter R.7.6 (version 4.0, July 2015).

Species and route selection

According to the test method EU B.56/ 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 4.0, July 2015) R.7a, chapter R.7.6.2.3.2.

You have also provided comments on the study design of the requested extended-one generation reproductive toxicity study addressing specifically the pre-mating exposure

period and the inclusion of cohort 1B animals.

Premating exposure period

ECHA understands that you would like to propose a shorter premating exposure duration because the result from the screening study and from repeated dose toxicity studies did not result effects on fertility or reproductive organs. You further indicated in your comments that *"If a 10 weeks premating period is nevertheless requested, it should be limited to the male animals and start dosing the female animals two weeks premating as requested by the OECD Guideline again for animal welfare reasons".*

The OECD test guideline 443 indicates that *"the duration of the pre-mating treatment in the Extended One-Generation Reproductive Toxicity Study is ... aimed at the detection of effects on functional changes that may interfere with mating behaviour and fertilisation."* and recommends that *"the pre-mating treatment should be sufficiently long to achieve steady-state exposure conditions in P males and females".* The OECD TG suggests that *"a 2-week pre-mating treatment for both sexes is considered adequate in most cases"* since *"for females, this covers 3-4 complete oestrous cycles and should be sufficient to detect any adverse effects on cyclicity."* and that *"for males, this is equivalent to the time required for epididymal transit of maturing spermatozoa and should allow the detection of post-testicular effects on sperm (during the final stages of spermiation and epididymal sperm maturation) at mating."*

You consider that ECHA's request for a 10-week premating exposure duration exceeds the recommendations in the OECD Guideline 443 and is not justified on the grounds of the existing data. You also point out that no effects on fertility were observed up to the highest dose of 250 mg/kg bw/day in the OECD TG 421 study and indicate that the highest test dose in an extended one-generation reproductive toxicity study would not exceed this dose level. On that basis the Registrant concluded that no effects on fertility in male rats are to be expected.

ECHA points out that the information requirement of Annexes IX and X, section 8.7.3 of the REACH Regulation, as investigated in the OECD TG 443 study, focuses on effects on fertility for both genders and the results should also be appropriate for classification and labelling purposes, which is reflected in the implementation of the flexible OECD TG 443 study design. This is highlighted in the recital (7) of the Commission Regulation (EU) 2015/282 of 20 February 2015 amending Annexes VIII, IX and X to the REACH Regulation as regards the extended one-generation reproductive toxicity study stating that *"It should be ensured that the reproductive toxicity study carried-out under point 8.7.3 of Annexes IX and X to Regulation (EC) No 1907/2006 will allow adequate assessment of possible effects on fertility. The premating exposure duration and dose selection should be appropriate to meet risk assessment and classification and labelling purposes as required by Regulation (EC) No 1907/2006 and Regulation (EC) No 1272/2008 of the European Parliament and of the Council."*

To achieve this, the premating exposure period must cover the spermatogenesis in male and folliculogenesis in females before mating. Thus, the concomitant investigations on functional fertility, sperm parameters and histopathology of reproductive organs after exposing all developmental stages of germ cells is necessary. This is further explained in ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a: Endpoint specific guidance, Version 4.1, October 2015 (http://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf)

which states: *"For the classification purpose, it is important to produce and evaluate the full spectrum of effects on fertility. Just to detect a most sensitive effect may not be enough for deciding on classification categorisation because full information on magnitudes, incidences, severity and types of all effects (MIST information) should be evaluated together to assist the decision."*

The Appendix R.7.6-3 to the above mentioned ECHA Guidance provides detailed guidance on setting the duration of the pre-mating exposure period. According to this Guidance, the default duration of the pre-mating exposure period is of 10 weeks in order to cover the full spermatogenesis and folliculogenesis before mating, allowing meaningful assessment of the effects on fertility. A shorter pre-mating exposure period may be justified based on substance-specific considerations.

ECHA highlights that the screening study (OECD TG 421) is designed to generated limited information concerning the effects of a test substance on reproductive toxicity is limited, as specified in the test guideline itself. Particularly, the premating exposure period in this study does not cover the full spermatogenesis cycle in male and folliculogenesis cycle in females before mating. Therefore, ECHA is of the opinion that whilst information obtained from a screening study may provide information on the potential of a substance to affect the reproductive performance, it does not provide comprehensive information on effects on spermatogenesis or folliculogenesis or fertility. ECHA considers that the arguments that you have brought forward in your comments do not constitute sufficient substance-specific information which would allow justifying a shorter premating exposure duration in an extended one-generation reproductive toxicity study. Therefore, ECHA has not amended the draft decision in this respect.

Inclusion of Cohort 1B

You indicated in your comments that you consider that the inclusion of cohort 1B in the design of this study as not necessary *"because all relevant parameters are sufficiently covered by cohort 1A"* and conclude that "Thus, cohort 1B is not required and should not be included due to animal welfare reasons". ECHA highlights that the inclusion of Cohort 1B in the design of the requested study is in accordance with the provisions of Annex X, 8.7.3 column 1 which require the inclusion of cohort 1B as part of the basic study design of the EOGRTS: *"Extended one-generation reproductive toxicity study (B.56 of the Commission Regulation on test methods as specified in Article 13(3) or OECD 443), basic test design (cohorts 1A and 1B without extension to include a F2 generation"*. The systematic inclusion of the cohort 1B in the design of the study is justified in the OECD TG 443 as follows: *"priority selection for follow-up assessment of reproductive performance by mating F1 animals, when assessed ..., and for obtaining additional histopathology data in cases of suspected reproductive or endocrine toxicants, or when results from cohort 1A are equivocal."* Thus, its inclusion allows, in this case, further investigations of equivocal findings on reproductive and endocrine organ/tissues in Cohort 1A animals. According to the OECD TG 443, the reproductive and endocrine organs in Cohort 1B animals should also be weighed and corresponding tissues processed to the block stage for potential further need. In addition, the statistical power of the information collected from Cohort 1 animals after weaning would be lower without Cohort 1B animals (e.g. for clinical signs, body weights, sexual maturation). Hence, your proposal to limit the study design to the cohort 1A does not comply with the REACH information requirement of Annex X, section 8.7.3 and cannot be accepted. Therefore, ECHA has not amended the draft decision in this respect.

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 EU B.56/ 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 some 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;

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 new information shows triggers which are described in column 2 of Section 8.7.3., Annex X and further elaborated in ECHA guidance. 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. The study design must be justified in the dossier and, thus, the existence/non-existence of the conditions/triggers must be documented.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH 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 sought to adapt this information requirement using the following justification: "*In accordance to Column 2 REACH Annex IX, long-term toxicity to aquatic invertebrates, information requirement 9.1.5, can be waived if no toxicity to aquatic organisms is expected. The short-term toxicity testing to aquatic invertebrates revealed that persulfates are practically non-toxic to aquatic invertebrates. Upon contact with water or water vapour substances of the Persulfate Category hydrolyse into cation and persulfate anion. Hydrolysis is temperature and pH dependent. Decomposition rates increase with decreasing pH value and increasing temperature.*

The persulfate anion, independent of the cation, undergoes further decomposition in normal water or acid conditions, readily oxidizing water to oxygen, producing sulphate and

hydrogen ions. All persulfate decomposition products are ubiquitous to the environment. Hydrolysis is metal catalyzed, and rapid reaction with organic matter is also possible. Therefore long-term toxicity testing of aquatic invertebrates is scientifically not justified."

In your technical dossier, you have provided eight short-term toxicity to aquatic invertebrates studies. In the marine study with saltwater invertebrate *Abra alba* according to PARCOM Ring test protocol (1993) with the registered substance diammonium persulfate (EC 231-786-5, CAS 7727-54-0) an EC50 (5 d) of 11 mg/L, most sensitive value available, was detected. Furthermore, the acute toxicity study to fish with diammonium persulfate (EC 231-786-5, CAS 7727-54-0) according to FIFRA guideline of the Pesticide Assessment revealed a LC50 (96 h) of 76.3 mg/L. Therefore, the persulfates cannot be considered as practically non-toxic to aquatic invertebrates as stated in the data waiver. Furthermore, in the absence of adequate data on hydrolysis, there is insufficient information available to conclude on the environmental exposure assessment or risk characterisation for the registered substance. Consequently, your justification for waiving does not meet the criteria of either the specific adaptation rules of Column 2 of Annex IX, section 9.1, or the general adaptation rules of Annex XI. Therefore, the adaptation 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.

In the comments to the draft decision you have agreed with the information requirement in the draft decision by stating the following "*The registrant agrees with ECHA to perform a study according to OECD 211 with one of the category member substances, preferably diammonium peroxodisulphate (see above for justification). Thus the registrant accepts ECHA's requirement (technical feasibility provided) but requests ECHA to reduce this information requirement to only one substance preferably diammonium peroxodisulphate*". ECHA has addressed your comments regarding the "Category approach for peroxodisulphates" in the other decisions on Sodium peroxodisulfate and Potassium peroxodisulfate.

According to ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 2.0, November 2014) 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.

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: Daphnia magna reproduction test (test method: EU C.20./OECD TG 211).

Notes for your consideration

According to ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4) if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. In such case, according to the integrated testing strategy, the Daphnia study is to be conducted first. If based on the results of the long-term Daphnia study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.

Due to the oxidation and hydrolysis in water and the influence of the pH conditions, 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 2.0, November 2014), 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).

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH 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 sought to adapt this information requirement using the following justification: "*In accordance to Column 2 REACH Annex IX, long-term toxicity to fish, information requirement 9.1.6, can be waived if no toxicity to aquatic organisms is expected. The short-term toxicity testing to fish revealed that persulfates are practically non-toxic to fish. Upon contact with water or water vapour substances of the Persulfate Category hydrolyse into cation and persulfate anion. Hydrolysis is temperature and pH dependent. Decomposition rates increase with decreasing pH value and increasing temperature. The persulfate anion, independent of the cation, undergoes further decomposition in normal water or acid conditions, readily oxidizing water to oxygen, producing sulphate and hydrogen ions. All persulfate decomposition products are ubiquitous to the environment. Hydrolysis is metal catalyzed, and rapid reaction with organic matter is also possible. Therefore long-term toxicity testing with fish is scientifically unjustified.*"

In your technical dossier, you have provided four short-term toxicity to fish studies. The key study, the acute toxicity study to fish with diammonium persulfate (EC 231-786-5, CAS 7727-54-0) according to FIFRA guideline of the Pesticide Assessment (1993) revealed a LC50 (96 h) of 76.3 mg/L. Therefore, the persulfates cannot be considered as practically non-toxic to aquatic invertebrates as stated in the data waiver.

Furthermore, in the absence of adequate data on hydrolysis, there is insufficient information available to conclude on the environmental exposure assessment or risk characterisation for the registered substance. Consequently, your justification for waiving does not meet the criteria of either the specific adaptation rules of Column 2 of Annex IX, section 9.1, or the general adaptation rules of Annex XI. Therefore, the adaptation cannot be accepted.
There were no indications in the dossier from the short-term toxicity studies on aquatic species that the fish would be substantially more sensitive than Daphnia.

In the comments to the draft decision you did not agree with the information requirement in the draft decision by stating the following reasons:
"*Long-term aquatic toxicity testing will be covered for the whole category with a new study according to OECD 211 with Daphnia. As already outlined by ECHA in the draft decision Daphnia is the more sensitive species for aquatic toxicity as compared to fish as shown by*

the large data set available for acute aquatic toxicity. Thus, it is not expected that the fish test will show lower toxicity as compare to Daphnia and will not improve the hazard assessment of the substance. Fish are vertebrates and testing with higher animals should only be done as a last resort taking account animal welfare reasons. ECHA noted in their draft decision that testing of long-term toxicity testing on fish according to ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4), should only be done if based on the results of the long-term Daphnia study and the application of a relevant assessment factor, no risks are observed PEC/PNEC<1).

In conclusion, the registrant requests ECHA to remove the testing requirement for a long-term toxicity testing on fish from the draft decision. Instead it should be noted, that testing of long term toxicity testing on fish is only required if the risk assessment conducted based on the new long-term daphnia study will result in no safe use (if PEC/PNEC>1)".

ECHA notes in the long-term Daphnia study above, ECHA stated the following "*In the marine study with saltwater invertebrate Abra alba according to PARCOM Ring test protocol (1993) with the registered substance diammonium persulfate (EC 231-786-5, CAS 7727-54-0) an EC50 (5 d) of 11 mg/L, most sensitive value available, was detected*". However, to establish substantial sensitivity between the species, a factor of 10 is recommended in the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R7b. There were no indications in the dossier from the short-term toxicity studies on aquatic species that the fish would be substantially more sensitive than Daphnia.

ECHA has indicated in both long-term aquatic toxicity testing that according to integrated testing strategy (ITS) the long-term toxicity testing on aquatic invertebrates (Daphnia) should be conducted first and that the results of this test should be considered together with other information as part of the chemical safety assessment to identify whether further long-term testing on fish is needed. This ensures that the Daphnia study is undertaken first to ensure no vertebrate animals are tested, unnecessarily. Following the Daphnia study, and the application of a relevant assessment factor, if no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted.

ECHA has addressed your comments regarding the "Category approach for peroxodisulphates" in the other decisions on Sodium peroxodisulfate and Potassium peroxodisulfate.
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 2.0, November 2014) fish early-life stage 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.

Regarding the long-term toxicity testing on fish pursuant to Annex IX, section 9.1.6.1, ECHA considers that the FELS toxicity test according to OECD TG 210 is the most sensitive of the standard fish tests available as it covers several life stages of the fish from the newly fertilised egg, through hatch to early stages of growth and should therefore be used (see

ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R7b, Figure R.7.8-4). The test method OECD TG 210 is also the only suitable test currently available for examining the potential toxic effects of bioaccumulation (ECHA Guidance Chapter R7b, version 2.0, November 2014). For these reasons, ECHA considers the FELS toxicity test using the test method OECD TG 210 as most appropriate and suitable.

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

According to ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4), if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. In such case, according to the integrated testing strategy, the Daphnia study is to be conducted first. If based on the results of the long-term Daphnia study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.

Due to the oxidation and hydrolysis in water and the influence of the pH conditions, 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 2.0, November 2014), 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).

9. Identification of DNELs and risk characterisation (Annex I, Sections 1.4. and 6.): Revise acute and long-term DNEL(s) for workers inhalation and dermal routes local effects using the default assessment factors and other recommendations of ECHA Guidance R.8 for DNEL derivation and revise the risk characterisation accordingly or provide a detailed justification for not using the recommendations of ECHA Guidance R.8 for DNEL derivation;

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation, the registration shall contain a chemical safety report which shall document the chemical safety assessment conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

Annex I, Section 1.4.1 of the REACH Regulation requires that the following factors shall, among others, be taken into account when deriving DNELs:
a) the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;
b) the nature and severity of the effect;
c) the sensitivity of the human (sub-)population to which the quantitative and/or qualitative information on exposure applies;
d) and that the DNELs reflect the likely route(s), duration and frequency of exposure.

The ECHA Guidance on information requirements and chemical safety assessment Chapter R.8 provides further details and specifically provides default factors which should be applied to derive DNELs in the absence of substance specific information to fulfil the REACH obligations.

ECHA notes that the assessment factors (AF) applied were not derived in accordance to the default assessment factors recommended in the ECHA Guidance R.8 for DNEL derivation.

Specifically, for local effects on the respiratory tract you have used an assessment factor of 1 for the remaining interspecies differences instead of the default AF of 2.5 and justified this deviation from the default AF by stated referring to the absence of "*evidence for differences in the general mode of action or kinetics*". ECHA points out that for effects on the respiratory tract, the ECHA Guidance R.8 recommends "*whether the mechanism indicates that the effect seen is a simple destruction of membranes due to the physico-chemical properties (e.g. pH) of the chemical concerned or whether a local metabolic process is involved, further kinetic and dynamic considerations still apply*" and that "*In such a situation, a chemical-specific remaining uncertainties factor or the default factor of 2.5 should be applied, as would be the case for systemic effects*". You have not provided substance-specific information to deviate from the default AF, therefore the default AF of 2.5 for remaining interspecies differences has to be used.
For long-term systemic effects via the inhalation route, you have used an AF of 1 for extrapolation from sub-chronic to chronic exposure whereas the default AF recommended in the ECHA Guidance R.8 for this duration extrapolation is 2. You have justified this deviation from the default AF by referring to "*the local nature of primary toxicity effects*". ECHA highlights that the ECHA Guidance R.8 specifies that in the absence of substance-specific information, the "*default assessment factors should be used for systemic effects and, in case of toxicity testing by inhalation, for local tissue damage in the respiratory tract*". Since no adequate substance-specific information has been provided to justify the deviation from the default AF, the default AF of 2 for extrapolation from sub-chronic to chronic exposure has to be used.

ECHA further points out that you have derived a DNEL for long-term dermal local effects by applying a route-to-route extrapolation from information on local toxicity obtained from an oral sub-chronic study. According to the ECHA Guidance on information requirements and chemical safety assessment, Chapter R.8 route-to-route extrapolation is not considered appropriate for local effects.

ECHA also notes that LD0/LC0 values have been used to derive the DNELs for acute toxicity. This is not in accordance with the recommendations from the ECHA Guidance on information requirements and chemical safety assessment, Chapter R.8 which recommends that LD50/LC50 should be used as point of departure for deriving DNELs for local toxicity, when available.

As explained above, the information provided on DNEL for the registered substance in the chemical safety report does not meet the general provisions for preparing a chemical safety report as described in Annex I, 1.4.1.

Consequently, you are given two options: you shall revise the DNELs for workers by applying the assessment factors recommended by ECHA that are appropriate in this case as specified above. Subsequently, you shall re-assess related risks.

In the alternative, you shall, in accordance with Annex I, Section 1.4.1, provide a full justification for the DNELs derived for workers provided in the chemical safety report by specifying how the following has been taken into account:
- the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;
- the nature and severity of the effect;
- the sensitivity of the human (sub-)population to which the quantitative and/or qualitative information on exposure applies;
- and that the DNELs reflect the likely route(s), duration and frequency of exposure.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to revise acute and long-term DNEL(s) for workers inhalation and dermal routes local effects using the default assessment factors and other recommendations of ECHA Guidance R.8 for DNEL derivation and revise the risk characterisation accordingly *or* provide a detailed justification for not using the recommendations of ECHA Guidance R.8 for DNEL derivation.

Notes for your consideration

The results of the studies requested with this decision shall be taken into account when revising the DNELs.

10. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation, the registration shall contain a chemical safety report which shall document the chemical safety assessment conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

Qualitative risk assessment

Annex I, Section 5. of the REACH Regulation indicates that the objective of the exposure assessment shall be to make a quantitative or qualitative estimate of the dose/concentration of the substance to which humans [...] are or may be exposed. The exposure assessment shall consider all stages of the life-cycle of the substance resulting from the manufacture and identified uses and shall cover any exposures that may relate to the identified hazards.

Further, Annex I, Section 6.5. of the REACH Regulation states that "*for those human effects and those environmental spheres for which it was not possible to determine a DNEL or a PNEC, a qualitative assessment of the likelihood that effects are avoided when implementing the exposure scenario shall be carried out.*"

In your CSR you state, "*Substances of the Persulfate Category were classified as sensitising, R 42/43 (may cause sensitisation by inhalation and skin contact) according to Directive 67/548/EEC(DSD), and Respiratory sensitisation, cat. 1 H334 (may cause allergy or asthma symptoms or breathing difficulties if inhaled) and skin sensitisation H317 (may cause an allergic skin reaction) according to Regulation 1272/2008/EC (CLP).*"

When a DNEL cannot be determined but hazards are identified, a qualitative assessment of the likelihood that effects are avoided when implementing the exposure scenario must be carried out (REACH Annex I, section 6.5). Practical Guide 15, "How to undertake a

qualitative human health assessment and document it in a chemical safety report" provides advice on how to do this.

Your registered substance is classified as a skin and respiratory sensitiser and, as such, a qualitative approach to the exposure assessment is required to ensure that the operational conditions and the risk management measures in the exposure scenarios accurately reflect what is required to protect workers and consumers. Many of the exposure scenarios contain uses where dermal exposure could be anticipated. By using a quantitative approach you have compared dermal exposure values, predicted through use of the ECETOC TRA and Consexpo, with DNELs derived from repeated dose toxicity studies. This is a flawed approach. A primary concern in the workplace and for consumers is to ensure that the likelihood of effects (skin and respiratory sensitisation in this case) is avoided when implementing the exposure scenarios. As such you should describe the steps to be taken and the risk management measures required to prevent exposure to the skin and to protect workers and consumers from inhalation effects. Currently your CSR contains no reference to procedures and methods other than through use of personal protective equipment and ventilation arrangements that still generate workplace levels of concern for sensitisation effects. For consumer uses, your CSR contains no reference tothe means to prevent exposure to the extent likelihood of effects are avoided.

Worker exposure

The exposure assessment produces estimates of exposure for the inhalation route and the dermal route for both solid forms and solutions, presumed to be aqueous. You have produced a full range of exposure estimates using the ECETOC TRA model and these have been compared with DNELs derived from repeated dose toxicity testing. However, for aqueous solutions, the exposure estimates are not correctly derived, as explained further below, and though you have derived risk characterisation ratios, they are not based on sound predictions of exposure. For dust exposures the estimates, up to 10 mg/m^3 outside of the use of respiratory protective equipment, indicate potential high levels of dust generation for some exposure scenarios. These high predicted levels, when estimated without use of RPE, may present a risk of sensitisation for both inhalation and especially through skin deposition.

The issue with the assessment relates to identification of measures to deliver an appropriate low level of exposure to be protective against respiratory and dermal sensitising effects. You identify both dermal and respiratory sensitisation has occurred in workers and this may be due to systemic effects resulting from skin challenge as much as from inhalation exposure – the mechanism of toxicity leading to these effects is not known.

Further, there is an inconsistency between the CSR outcome of hazard assessment and the guidance on safe use. In the Section 11 of IUCLID, Guidance on safe use, you state, "*The product contains no ingredients which have to be monitored and controlled for working place exposure limits. General dust exposure limits: 10 mg/m³ (respirable fraction), 3 mg/m³ (alveolar fraction);* this clearly does not take account of the sensitising potential for these substances or even your own proposed DNEL of 2.06 mg/m^3 for long term systemic effects.

The worker long term inhalation DNEL of 2.06 mg/m^3, based on repeat dose toxicity, may not be protective against sensitisation effects and risk management measures need to ensure control at a lower level. This requires a qualitative approach with, for inhalation exposure, a prudent target concentration to help determine the correct RMMs and to ensure

conditions in the workplace do not generate dust levels that can lead to significant deposition on the exposed skin.

Estimates of inhalation exposure of aqueous solutions

For aqueous solutions you have used the ECETOC TRA model beyond its boundaries of applicability in that estimates of exposure have been provided for liquid formulations where it is unclear how such estimates have been derived when the registered substance is dissolved in water. ECETOC Technical Report 114, Table 3 (page 16) clarified the domain of reliable application of the ECETOC TRA worker model and made a clear statement that it cannot predict exposures to solids suspended or dissolved in liquids. However, the substance, as such, has an extremely low vapour pressure associated with an ionic solid. Consequently inhalation exposures from handling aqueous solutions, other than for spraying tasks, would be anticipated to be insignificant. The ECETOC TRA provides an output based on the volatility of the substance, but, it is of limited value to assess inhalation exposure for aqueous solutions and this leads to erroneous proposals for risk management measures. Further, ECETOC Technical Report 114 states the model does not reliably predict aerosol exposures. Though the model will provide an exposure output, it is not clear how this may correspond to exposure that may actually be anticipated for such spraying tasks.

Estimates of dermal exposure of aqueous solutions.

Dermal exposure estimates have mostly been calculated using the ECETOC TRA worker tool version 2 with the local exhaust ventilation modifier included in the assessment. Although this may have some relevance to dermal exposure from handling a dusty solid, the local exhaust ventilation modifier should not be used for predicting exposures for tasks involving aqueous solutions, e.g. from dipping articles, as residues are not volatile and are likely to remain on surfaces. According to ECETOC's own guidance the predictions for aqueous solutions are questionable in any case. The use of the local exhaust ventilation modifier is specifically advised against in the ECHA Guidance on information requirements and chemical safety assessment R.14, chapter R.14.4.8 (version 2.1, November 2012), page 21.

Risk management measures

In section 11 of the IUCLID file, Guidance on safe use, you only specify butyl rubber gloves; the CSR proposes *rubber or PVC or other plastic material gloves, glove thickness: 0.5 mm, break through time: >= 8 h*. This provides a confusing picture of which gloves should be used. Thickness is generally specified by manufacturers for each glove type and varies. Protective clothing standards are not specified in the CSR or guidance on safe use. Within each exposure scenario you specify *"Light weight protective clothing" and "Wearing of protective clothing/personal protective equipment is mandatory."* Annex II requires *"taking into account Council Directive 89/686/EEC and referring to the appropriate CEN standard detailed specifications shall be given on which equipment will provide adequate and suitable protection, including ... if it is necessary to protect a part of the body other than the hands, the type and quality of protection equipment required shall be specified, such as gauntlets, boots, bodysuit based on the hazard associated with the substance."*

Annex II Section 0.1.2. requires this information to be consistent with that provided in the CSR. Given that the substance can potentially take a liquid or solid form, then different types of clothing will be required, depending on its use. These forms of clothing are commonly designated as Type 4 (liquid spray), Type 5 (solid) and Type 6 (liquid splash) and are covered by specific European standards. This information should be available in the CSR

and/or the Guidance on Safe Use and is important information for a proven sensitising substance used both as a dusty solid and in aqueous solution.

Consumer exposure

The available exposure assessment contains estimates of exposure for the inhalation route and the dermal route for both solid forms and solutions for swimming pools and spas treatment (PC 37), and viscous liquid mixtures for metal surface treatment products (PC 14). You have produced a full range of exposure estimates using the Consexpo model and these have been compared with DNELs derived from repeated dose toxicity testing. However, only the exposure to vapour was estimated but not the exposure to dust. Based on the information provided in the registration dossier dust can be expected to be present and it may present a risk of respiratory sensitisation therefore exposure to this form of the substance should be estimated.

Furthermore, the provisions of Annex I, section 5.2.4 of the REACH Regulation require that "*In particular, the exposure estimation shall take account of: ... transformation and/or degradation products*". ECHA notes that for both consumer scenarios no information was given on potential hazardous transformation and/or degradation products. ECHA also observes that no exposure during the post-application stage was established for the use as surface metal treatment whereas according to the provisions of Annex I, section 5.2.2 of the REACH Regulation all stages of the life cycle of the substance. Consequently the exposure during the post-application phase is not adequately addressed and the control of the risk of skin sensitisation is not ensured.

On the basis of the information provided, the exposure assessment for dermal exposure during the mixing/loading and application phases suggests non-negligible level of exposure that may present a risk of skin sensitisation. The consumer long term inhalation DNEL of 1.03 mg/m3 and dermal DNEL of 9.1 mg/kg bw/day, based on information obtained from repeated dose toxicity studies, may not be protective against sensitisation effects through inhalation and dermal routes. According to the provisions of Annex I, section 6.5, practical risk management measures (product-integrated measures) are needed to ensure control of the exposure at all time to protect consumers against skin and respiratory sensitisation.

In the comments to the draft decision you have agreed to address the information requirement in the next update and stated the following "*The registrant took note of ECHA's comments but does not fully agree. Nevertheless, the registrant will address ECHA's requests in the next update including conclusive qualitative measures to show safe use of the substance with regard to local effects like skin and respiratory sensitization. The update will be done taking into account ECHA's current guidelines.*"

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to provide a qualitative exposure assessment demonstrating the likelihood that effects for respiratory and skin sensitisation are avoided for all identified uses and to detail the operational conditions and risk management measures and revise the exposure assessment and risk characterisation accordingly.

11. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: revise the environmental exposure estimation and risk characterisation

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation the registration shall contain a chemical safety report (CSR) which shall document the chemical safety assessment (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

According to Article 14(4) of the REACH Regulation, if the substance fulfils the criteria for any of the hazard classes of Annex I to Regulation (EC) No 1272/2008 listed in Article 14(4) of the REACH Regulation or is assessed to be a PBT or vPvB, the chemical safety assessment shall include an exposure assessment and risk characterisation. ECHA notes that the registered substance is classified as:

- H272 May intensify fire; oxidiser
- H302 Harmful if swallowed
- H315 Causes skin irritation
- H317 May cause an allergic skin reaction
- H319 Causes serious eye irritation
- H334 May cause allergy or asthma symptoms or breathing difficulties if inhaled
- H335 May cause respiratory irritation.

Therefore an exposure assessment and risk characterisation shall be included in the chemical safety assessment.

The exposure assessment shall be carried out according to section 5 of Annex I and shall include exposure scenarios and exposure estimations for the registered substance. The exposure assessment shall consider all stages of the life-cycle of the substance resulting from the manufacture and identified uses and shall cover any exposures that may relate to the identified hazards. Annex I, section 6 of the REACH Regulation requires you to characterise the risk for each exposure scenario.

In your dossier you present 5 exposure scenarios (ES):

- ES0: Manufacturing
- ES1: Formulation
- ES2: Industrial use
- ES3: Professional use
- ES4: Consumer use (General public)

The environmental exposure assessment and risk characterisation you have provided contain several deficiencies as indicated below.

a) Absence of adequate justification for the release factors applied for ES0, ES1 and ES2

Pursuant to Annex I, section 5.1.1 of the REACH Regulation, exposure scenarios (ES) shall include, where relevant, a description of operational conditions (OCs) and of risk management measures (RMMs). As indicated in Annex I, section 5.2.2. of the REACH Regulation, emission estimation shall be performed under the assumption that the risk management measures and operational conditions described in the exposure scenario have been implemented. These RMMs and OCs should be included in the exposure scenarios provided in a CSR.

According to the Guidance on information requirements and chemical safety assessment Chapter R.16: Environmental Exposure Estimation (ECHA, version: 2.1, October 2012), operational conditions "*consist of a set of actions, tools, parameters such as amount of substance, process temperature and pH, duration and frequency of release, type of use (e.g. indoor or outdoor), containment of process (open or closed), continuous or batch process (leading to an intermittent release), capacity of surroundings, etc. having, as a side effect, an impact on the release and the exposure*". Risk management measures "*consist of technologies and procedures aimed at either reducing the releases and/or preventing a release pathway. Examples of risk management measures intended to reduce release are filters, scrubbers, biological or physico-chemical wastewater treatment plants etc.*" Both OCs and RMMs have an impact on the type and amount of release and the resulting exposure.

The release factors associated with Environmental Release Categories (ERCs) cited in ECHA guidance R.16 can be used for a first tier assessment of the emissions. However, better information may be available that could then be used instead. In particular, release factors can be refined by taking into account RMMs and OCs. In this case, it is important to explicitly link such RMMs and OCs to the release factors and communicate them properly to the downstream users in the exposure scenarios.

You have used release factors that deviate from those recommended in ECHA guidance R.16. for exposure scenarios ES0, ES1 and ES2. In an annex to your CSR, you have provided the EUSES full report which details the releases factors you have used for your assessment. ECHA notes that you have used release factors that deviate from those recommended in ECHA guidance R.16. for exposure scenarios ES0, ES1 and ES2.

For ES0 (Manufacturing), you have assumed the following release factors: 5E-5 (0.005%) for air, 6E-5 (0.006%) for water and 0 for soil. The ERC to which you refer for this exposure scenario is ERC1: "*Manufacture of chemicals*". By comparison, the default release factors recommended in ECHA Guidance R.16 for ERC1 are: 5E-2 (5%) for air, 6E-2 (6%) for water and 1E-4 (0.1%) for soil.

For ES1 (Formulation), you have assumed the following release factors: 2.5E-4 (0.025%) for air, 2E-4 (0.02%) for water and 1E-6 (0.0001%) for soil. The ERC to which you referred for this exposure scenario is ERC2: "*Formulation of mixtures*". By comparison, the default release factors recommended in ECHA Guidance R.16 for ERC2 are: 2.5E-2 (2.5%) for air, 2E-2 (2%) for water and 1E-4 (0.01%) for soil.

For ES2 (Industrial use), you make reference to several ERCs:

- For ERC6a ("*Industrial use of intermediate*"), you have assumed the following release factors: 5E-4 (0.05%) for air, 0 for water and 0 for soil. By comparison, the default release factors recommended in ECHA Guidance R.16 for ERC6a are: 5E-2 (5%) for air, 2E-2 (2%) for water and 1E-3 (0.1%) for soil.
- For ERC6b ("*Industrial use of reactive processing aids*"), you have assumed the following release factors: 1E-4 (0.01%) for air, 0 for water and 0 for soil. By comparison, the default release factors recommended in ECHA Guidance R.16 for ERC6b are: 1E-3 (0.1%) for air, 5E-2 (5%) for water and 2.5E-4 (0.025%) for soil.
- For ERC6d ("*Industrial use of auxiliaries for polymerisation*"): 3.5E-4 (0.035%) for air, 0 for water and 0 for soil. By comparison, the default release factors recommended in ECHA Guidance R.16 for ERC6a are: 3.5E-1 (35%) for air, 5E-5 (0.005%) for water and 2.5E-4 (0.025%) for soil.

ECHA considers that you have not provided any satisfactory justifications for using these release factors. You claim that risk management measures with removal efficiency of 99.9% (for ES0), 99% (for ES1 in air, water and soil), 99% (for ES2 in air and ERC6a), 90% (for ES2 in air and ERC6b), 99.9% (for ES2 in air and ERC6d) are in place. However, you have not provided any technical details on how such high removal efficiencies could be achieved.

For example, for releases to water, you claim that the waste water is "*neutralised and detoxified*" but you have not provided any more explanation (by what mechanism or procedure is the substance "*neutralised and detoxified*"?). The substance is very soluble, not volatile, not biodegradable and is assumed to have a hydrolysis half-life of 80.35 days, therefore ECHA considers that removal of the registered substance for example in a waste water treatment plant will be actually quite limited.

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation, you are requested to revise release factors for exposure scenarios ES0, ES1 and ES2 in order to ensure that either the default ERC release factors recommended in ECHA Guidance R.16 are used or that any non-default ERC release factors are adequately justified (e.g. based on risk management measures).

b) Absence of adequate information on the assumed "fraction of the main source" (i.e. annual use at a site)

Pursuant to Annex I, section 5.2.1 of the REACH Regulation the exposure estimation entails three elements: emission estimation, assessment of chemical fate and pathways and estimation of exposure levels. Pursuant to Annex I, section 5.2.2. of the REACH Regulation, emission estimation shall consider the emissions during all relevant parts of the life-cycle of the substance resulting from the manufacture and each of the identified uses.

For point sources, a protective estimation of the emissions requires that the capacity of the largest point source for the particular stage of the life cycle be estimated. The main source thus represents the emission source where the largest fraction of the production volume or market volume of the substance is handled. If this information is not known, it has to be estimated from the registered total annual tonnage.

For ES0 (Manufacturing), you have assumed that the fraction of the main local source is 60% of the registered total annual tonnage. For ES1 (Formulation) and ES2 (Industrial use), you have assumed a fraction of 10% of the registered total annual tonnage.

The Guidance on information requirements and chemical safety assessment Chapter R.16: Environmental Exposure Estimation (ECHA, version: 2.1, October 2012, page 15) recommends that, for an industrial site, the annual use at the site be set, by default, to 100% of the total annual tonnage for the use, i.e. that the fraction of the main source be set to 100%. Exposure scenarios ES0, ES1 and ES2 all apply to industrial sites, and therefore by default the annual use at a site should have been assumed to be 100% for these 3 exposure scenarios. This default value of 100% is a worst case to cover situations where the total registered tonnage is processed by at a single site. By assuming lower values, you may underestimate the local exposure.

The ECHA guidance specifies that the default value of 100% can be overwritten, on the basis of site specific information or of information on the actual amount used by the largest downstream user (ECHA guidance R.16, pages 18-19). However no such information is provided in the dossier, and you have not provided any justification for deviating from the default recommendation of the guidance.

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation, you are requested to apply a "fraction of the main source" of 100% for exposure scenarios ES0, ES1 and ES2 in accordance with the recommendations of ECHA Guidance R.16 or to provide adequate justification for any deviation from these recommendations.

c) Absence of justification for the dilution factors for freshwater and marine water

Pursuant to Annex I, section 5.2.4. of the REACH Regulation, exposure estimation shall take account of spatial and temporal variations in the exposure pattern.

Chapter R.16.6.6.2 of the ECHA Guidance on information requirements and the chemical safety assessment (ECHA, version: 2.1, October 2012) recommends that the default dilution factor for sewage from municipal treatment plants emitted to a freshwater environment be 10. For discharges to a coastal zone (marine environment) the recommended default dilution factor is 100.
For ES0 and ES1, you have applied dilution factors of 100 for freshwater and 1000 for coastal water. These deviate from the recommendation of ECHA guidance R.16.

These default values recommended in the ECHA guidance are assumed to be representative for a realistic worst case taking account of spatial and temporal variations. The guidance specifies that higher dilution factors can be applied if this can be founded by site-specific information. However you have not provided any such justification.
Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation, you are requested to amend your exposure assessment for exposure scenarios ES0 and ES1 by using the default dilution factors recommended in ECHA Guidance R.16 for freshwater and coastal water or to provide adequate justification for deviating from those recommendations.

d) Absence of adequate justification on PECs for freshwater and marine water used for the risk assessment

Pursuant to Annex I, section 5.2.1 of the REACH Regulation the exposure estimation entails three elements: emission estimation, assessment of chemical fate and pathways and estimation of exposure levels. Annex I, section 5.2.5. of the REACH Regulation specifies that appropriate models can be used for the estimation of exposure levels. Pursuant to Annex I, section 6.3, the risk characterisation for the environment consists of a comparison of the predicted environmental concentrations (PEC) in each environmental sphere with the predicted no-effect concentrations (PNEC).

ECHA notes that, for exposure scenario ES0 (Manufacturing), you have used for your risk assessment, and more specifically for the calculation of the risk characterisation ratios, a PEC of 0.0104 mg/L for freshwater and of 9.66E-4 mg/L for marine water. However, according to the EUSES full report provided in an annex to the CSR and section 9.1 of the CSR, the PECs calculated for ES0 should be respectively 0.0122 mg/L for freshwater and 2.76E-3 mg/L for marine water. You have not provided any explanation for that discrepancy.

Transparent documentation and in particular all input parameters used for the modelling are provided in the EUSES full report, therefore ECHA considers that the PEC values of 0.0122 mg/L for freshwater and 2.76E-3 mg/L for marine water presented in the EUSES full report for exposure scenario ES0 are justified. However the PEC values of 0.0104 mg/L for freshwater and of 9.66E-4 mg/L for marine water that are actually used for your risk

assessment do not have any justification and therefore ECHA considers that the risk characterisation ratios you have calculated for exposure scenario ES0 are not appropriate.

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation, you are requested to amend your exposure assessment and risk characterisation for exposure scenario ES0 by using PEC values that are adequately justified and consistent with the input parameters used for the modelling.

e) Absence of adequate justification for the selection of $PNEC_{soil}$ used for the risk assessment

Pursuant to Annex I, section 3.3 of the REACH Regulation, a predicted no-effect concentrations (PNEC) shall be established for each environmental sphere. Pursuant to Annex I, section 6.3, the risk characterisation for the environment consists of a comparison of the predicted environmental concentrations (PEC) in each environmental sphere with the PNECs.

ECHA notes that you have derived a $PNEC_{soil}$ of 1.32E-2 mg/kg ww. However for the risk assessment for exposure scenarios ES0 (Manufacturing) and ES1 (Formulation), and in particular for the calculation of the risk characterisation ratios for the terrestrial compartment, the $PNEC_{soil}$ you have actually used is 10 times higher (1.3E-1 mg/kg ww). The $PNEC_{soil}$ value of 1.32E-2 mg/kg ww has been derived using the equilibrium partitioning method, and you have provided the corresponding equations and input parameters. Therefore, ECHA considers that this value of 1.32E-2 mg/kg ww is properly documented. However, ECHA notes that you have no justification for the value of 1.3E-1 mg/kg ww actually used for the risk assessment. Therefore ECHA considers that the risk characterisation ratios for the terrestrial compartment and for exposure scenarios ES0 (Manufacturing) and ES1 (Formulation) are not appropriate.

In the comments to the draft decision you agreed to address the information requirement in the next update and stated the following "*The registrant took note of ECHA's comments but does not fully agree. Nevertheless, the registrant will address ECHA's requests in the next update (release fractions of the main source, dilution factors, used PECs and PNECs,). In addition, the lead registrant is not responsible to cover all downstream user uses by conducting a downstream user or market survey according to the REACH legislation. In contrast, the registrant is obliged to define conditions of safe use and communicate them to the downstream users via an eSDS. This was done by the registrant. If any of the downstream users does not fulfil the RMMs and OCs given in the CSR/eSDS he has to get back to the registrant and should ask for a refinement or to perform his own downstream user risk assessment to show safe use according to the REACH legislation (obligations of DUs)*". ECHA notes that you have outlined your interpretation of the REACH obligations to Registrants and downstream users. ECHA considers this information outside the information requirement in question.
Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation, you are requested to amend the risk characterisations for exposure scenarios ES0 and ES1 by using a $PNEC_{soil}$ value that is adequately justified.

12. Deadline to submit the requested information in this decision

In the draft decision communicated to you the time indicated to provide the requested information was 36 months from the date of adoption of the decision. In your comments on the draft decision, you requested an extension of the timeline to 48 months. You sought to justify this request by referring to the time required for sequential performance of both pre-natal developmental toxicity studies, including the relevant dose-range finding studies, the extended one-generation reproductive toxicity study and taking into account the laboratory capacity for conducting these studies. ECHA evaluated the justification provided and decided to change the deadline from 36 months to 48 months. The present decision was modified.

In this specific case, further to a proposal for amendment submitted by a national competent authority, and considering the skin and respiratory sensitising properties of the substance, the deadline set in this decision has been split in 2 deadlines. The information on a qualitative exposure assessment for workers and consumer uses is to be provided within 6 months of this decision in order to ensure adequate protection of the health of workers and consumers without undue delay, while the deadline to provide the other information requested in this decision is maintained to 48 months.

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 October 2015.
ECHA notified you of the draft decision and invited you to provide comments.

ECHA took into account your comments and did not amend the request(s). ECHA took into account your comments and amended the deadline.

ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment.

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

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

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation:

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 during its MSC-48 meeting 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 request(s) in this decision, or to fulfil otherwise the information requirement(s) 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 substance used for the new test(s) 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 composition 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 substance tested in the new test(s) 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 test(s) must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.

4. Article 13(1) of the REACH Regulation provides that information shall be generated whenever possible by means other than vertebrate animal tests.

   In relation to the grouping of substances and read-across approach, please note that ECHA has accepted this approach for some endpoints which are not addressed in the draft decision, e.g. sub-chronic toxicity (90-days). However, as explained in Appendix 1 of the draft decision, ECHA has concluded that for some endpoints there is either no information available or that the information provided is not adequate or reliable for the purpose of fulfilling the corresponding information requirement.

   Similar compliance check decisions requesting the missing information have been/will be sent to all lead registrants of the category members.

   In order to generate the requested information you should consider whether or not the grouping of substances and read-across approach applied within the category can also be applied to the information requirements requested in the draft decision or whether it is necessary to generate information separately for each of the registered member substances of the category.

   If you consider that the grouping and read-across approach can be applied you should together with the other lead registrants of the category agree to identify the test material(s) which you consider to be the most representative of the category for fulfilling the information requested in the present decision. Justification will need to be provided for the choice of test material(s).