Helsinki, 15 November 2019

Addressee: [redacted]

Decision number: CCH-D-2114488748-25-01/F
Substance name: Fatty acids, C18 (unsaturated), reaction products with diethylenetriamine
EC number: 629-715-1
CAS number: 1226892-43-8
Registration number: [redacted]
Submission number: [redacted]
Submission date: 18/05/2018
Registered tonnage band: over 1000[1]

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

2. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route with the registered substance specified as follows:**
   - **Ten weeks premating exposure duration for the parental (P0) generation;**
   - **Dose level setting shall aim to induce systemic toxicity at the highest dose level;**
   - **Cohort 1A (Reproductive toxicity);**
   - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation); and**
   - **Cohort 3 (Developmental immunotoxicity).**

3. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: Alga, growth inhibition test, EU C.3./OECD TG 201) with the registered substance using the standard test media (i.e. without added DOC/DOM or suspended matter)**

4. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with the registered substance using the standard test media (i.e. without added DOC/DOM or suspended matter)**

5. **Sediment simulation testing (Annex IX, Section 9.2.1.4.; test method: Aerobic and anaerobic transformation in aquatic sediment systems, EU C.24./OECD**

[1] There are members in the joint submission, which have registered the substance at the tonnage level of 1 000 tonnes or more per year.

TG 308) at a temperature of 12 °C with the registered substance.

The biodegradation of each relevant constituent present in concentration at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study;

6. **Identification of degradation products (Annex IX, Section 9.2.3.)**

7. **Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD TG 305-III, dietary exposure) with the registered substance. The bioaccumulation of each relevant constituent present in concentration at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study;**

8. **Long-term toxicity to sediment organisms (Annex X, Section 9.5.1.); using one or more of the following test methods: Sediment-water Chironomid toxicity using spiked sediment (OECD TG 218) or Sediment-water Lumbriculus toxicity test using spiked sediment (OECD TG 225) or Sediment-Water Chironomid Life-Cycle Toxicity Test Using Spiked Sediment (OECD TG 233) with the registered substance;**

9. **Identification of PNEC and risk characterisation (Annex I, Section 3.3.1. and 6.): revise PNECs for freshwater, marine water, intermittent releases, freshwater sediment and marine sediment**

   - using the study giving rise to the highest concern according to Annex I, Section 3.1.5 and revise the risk characterisation accordingly *or* provide a detailed justification for not using the study giving rise to the highest concern;

   - using the assessment factors recommended by ECHA and revise the risk characterisation accordingly *or* provide a detailed justification for not using the recommendations of ECHA guidance in PNEC derivation.

10. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment:**

    - **use default release factors and revise the risk characterisation accordingly *or* provide a detailed justification for not using the default release factors, for instance based on risk management measures, operational conditions or substance properties;**

11. **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 exposure scenarios and detail the operational conditions and risk management measures and revise the exposure assessment and risk characterisation accordingly.**

You have to submit the requested information in an updated registration dossier by ***23 May 2022***. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

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

Appeal

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

Authorised[2] by Wim De Coen, Head of Unit, Hazard Assessment.

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

Appendix 1: Reasons

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

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

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

The technical dossier contains information on pre-natal developmental toxicity study in rat by the oral route using the registered substance as test material (study report, 2014). You have also provided study records for two pre-natal developmental toxicity studies in rats with analogous substance, Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl) Me sulfate) (EC no: 268-531-2, CAS no: 68122-86-1) (publication, 1992 and 1993).

However, there is no information provided for a pre-natal developmental toxicity study in a second species. Instead, you have provided the following information in the technical dossier: *"The low likelihood of exposure follows from its use limited to industrial and professional users where following its corrosive and sensitising properties will provide for sufficient protection measures to prevent exposure. The likelihood of exposures via inhalation is low considering the high boiling point (> 300 °C) and very low vapour pressure (0.00017 mPa at 25°C) and use applications that do not involve the forming of aerosols, particles or droplets of an inhalable size. In view of low potential of exposures in combination with an overall low level of toxicity, and a total lack of effects observed in reproductive parameters from developmental toxicity and reproduction screening studies within the group of AAI, and no effects on reproductive organs observed in available repeated dose studies, further developmental toxicity studies in a second species is not indicated".*

ECHA understands that while you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to the general rules of adaptation according to Annex XI, Section 3.2. (a) and (b).

ECHA has first evaluated your adaptation based on the conditions specified in Annex XI, Section 3.2.(a) (i), and (ii), and (iii). Please note that all these three conditions must be fulfilled.

- The condition in Annex XI, Section 3.2.(a) (i) requires to demonstrate the absence of or no significant exposure in all scenarios of the manufacture and all identified uses. You have justified 'low likelihood of exposure' of the substance due to 'its use limited to industrial and professional users'. However, based on the information provided in the CSR and the use description of the substance, there are scenarios with potential for exposure (e.g., PROC 8b). For example, for PROC 8b ECHA notes a RCR for combined worker exposure of [redacted] indicating that exposure takes place. Hence, you have not demonstrated the absence of or no significant exposure for the full life cycle of the substance. Therefore, ECHA considers that the general rules for adaptation

according to Annex, Section 3.2. (a) (i) are not met.

- The condition in Annex XI, Section 3.2.(a) (ii) requires to derive DNEL for reproductive toxicity from the available test data for the substance concerned taking full account of the increased uncertainty resulting from the omission of the information requirement, and the derived DNEL is relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes. ECHA notes that you have derived the DNEL for reproductive toxicity from the OECD TG 422 study ([redacted], 2010).

  However, according to the footnote of Annex XI, Section 3.2.(a) (ii) a DNEL derived from the a screening test for reproductive/developmental toxicity shall not be considered appropriate to omit an extended one-generation reproductive toxicity study. Hence, ECHA considers that the general rules for adaptation according to Annex, Section 3.2. (a) (ii) are not met.

- The condition in Annex XI, Section 3.2.(a) (iii) requires the comparison of the derived DNEL with the results of the exposure assessment shows that exposures are always well below the derived DNEL. However, the RCR derived for some of exposure scenarios (e.g., PROC 8b) shows that exposure may not be well below the derived DNEL. Hence, ECHA considers that the general rules for adaptation according to Annex, Section 3.2. (a) (iii) are not met.

Thus, ECHA considers that the conditions specified in the adaptation according to Annex, Section 3.2.(a) is not met, and consequently your adaptation is rejected.

Secondly, ECHA has evaluated your adaptation according to Annex XI, Section 3.2.(b). Pursuant to Section 3.2.(b) of Annex XI, you have to demonstrate and document for all relevant scenarios that throughout the life cycle of the substance strictly controlled conditions as set out in Article 18 (4) (a) to (f) are fulfilled. Article 18(4)(a) requires that "*the substance is rigorously contained by technical means during its whole lifecycle including manufacture, purification, cleaning and maintenance of equipment, sampling, analysis, loading and unloading of equipment or vessels, waste disposal or purification and storage*". However, in the dossier you have not confirmed that the registered substance is used in accordance with conditions set out in Article 18(4)(a) to (f). The dossier does not contain information which would demonstrate that the substance is rigorously contained by technical means during its whole lifecycle, and no description is given of how strictly controlled conditions are ensured. Hence, the conditions specified in the adaptation of Annex XI; Section 3.2.(b) is not met, and consequently your adaptation is rejected.

Furthermore, your claim of there is "*an overall low level of toxicity*" is not demonstrated in the provided studies conducted in rat due to the following reasons:

(1) The pre-natal developmental toxicity study (study report, 2014) resulted in maternal toxicity at 150 mg/kg bw/day such as "*reduced body weight*", and two dams showed macroscopic abnormaties in gastrointestinal tract and also in other organs, e.g thymus and spleen).
(2) The reproductive/ developmental screening study ([redacted], 2010) showed parental toxicity at 100 mg/kg bw/day such as "*increased incidence/severity of macrophage foci in the mesenteric lymph node at both the end of treatment and recovery period in males*", and "*lower prostate and seminal vesicle weight, and lower prostate to body weight ratio*".
(3) In the 90-day study, the "*presence of foamy macrophages in the lamina propria of*

the small intestines and mesenteric lymph nodes is observed, as well as lower mean body weight and body weight gain" at the 30 and 100 mg/kg bw/day.

You also claim *"a total lack of effects observed in reproductive parameters from developmental toxicity and reproduction screening studies within the group of AAI, and no effects on reproductive organs observed in available repeated dose studies, further developmental toxicity studies in a second species is not indicated".* However, you are required to support your claim of lack of developmental effects in the second species with data that investigates the pre-natal developmental toxicity of the registered substance in a second species.

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.

The test in the first species was carried out by using a rodent species (rat). According to the test method OECD 414, the rabbit is the preferred non-rodent species. On the basis of this default assumption, ECHA considers that the test should be performed with rabbit as a second species.

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

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you recognise that the request may be a requirement for an Annex X dossier and based on your knowledge, the exposure to the substance in the industrial setting is insignificant. In addition, you have indicated your intention to further develop exposure assessment and to evaluate the adaptation possibilities according to Annex X and XI.

For all the reasons specified above, the information in the CSR indicates potential exposure (e.g., PROC 8b). You have not provided new information in your comments on the draft decision that would show that any of the adaption rules are met.

As specified on page 1 above, the compliance check is based on the highest tonnage band of the joint submission to determine the information requirements that apply to the registration.

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

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

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

in the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).
Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

a) The information provided

You have not provided any study record of an extended one-generation reproductive toxicity study in the dossier that would meet the information requirement of Annex X, Section 8.7.3.

Instead, you have provided the following information in the technical dossier:

- End-point study record 1: Key study: screening for reproductive / developmental toxicity, rat, oral (OECD TG 422; GLP) with registered substance, [redacted] 2010 (study report), rel 1.

- End-point study record 2: *The low likelihood of exposure can be considered as its use is limited to industrial and professional users where following its corrosive and sensitising properties will provide for sufficient protection measures to prevent exposure. The likelihood of exposures via inhalation is low considering the high boiling point (> 300 °C) and very low vapour pressure (0.00017 mPa at 25°C) and use applications that do not involve the forming of aerosols, particles or droplets of an inhalable size. In view of low potential of exposures in combination with an overall low level of toxicity, and a total lack of effects observed in reproductive parameters from developmental toxicity and reproduction screening studies within the group of AAI, and no effects on reproductive organs observed in available repeated dose studies, a 2-generation study is not considered necessary."*

ECHA understands that while you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to the general rules of adaptation according to Annex XI, Section 3.2 (a) and (b). However, for all the resons explained above under request 1, your adaptations of the information requirement according to Annex XI, Section 3.2.(a) and (b) are rejected.

Furthermore, your claim of *"an overall low level of toxicity"* is not demonstrated in the provided studies conducted in rat for all the resons explained above under request 1. You also claim a *"total lack of effects observed in reproductive parameters from developmental toxicity and reproduction screening studies within the group of AAI, and no effects on reproductive organs observed in available repeated dose studies, a 2-generation study is not considered necessary".* However, the available data do not allow to conclude on absence of reproductive effects, because such studies do not provide equivalent information on sexual function and fertility, and effects on offspring (information on development and toxicity of the offspring from birth until adulthood due to pre-and postnatal and adult exposure in the F1 generation) compared to an extended one-generation reproductive toxicity study according to OECD TG 443.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you recognise that the request may be a requirement for an Annex X dossier and based on your knowledge the exposure to the substance in the industrial setting is insignificant. In addition, you have indicated your intention to further develop exposure assessment and to evaluate the adaptation possibilities according to Annex X and XI.

For all the reasons specified above, the information in the CSR indicates potential exposure (e.g., PROC 8b). You have not also provided new information during your comments on the draft decision that would show that any of the adaption rules are met.

As specified on page 1 above, the compliance check is based on the highest tonnage band of the joint submission to determine the information requirements that apply to the registration.

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. 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.

b) The specifications for the study design

Premating exposure duration and dose-level setting

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

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

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

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

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you have stated that before conducting the study it is relevant to assess all available data and in particular the registered substance is corrosive and testing at concentration/dose causing corrosion shall be avoided.

ECHA acknowledges your comments and agrees that it is crucial to take into account all available information on the registered substance's properties before commencing the study. Specifically, as the registered substance is corrosive, the highest dose shall be selected with the aim to avoid unnecessary animal suffering.

Cohort 3
The developmental immunotoxicity Cohort 3 needs to be conducted in case of a particular concern on (developmental) immunotoxicity.

One of the Member State Competent Authorities submitted a proposal for amendment (PfA) explaining that the conditions for triggering Cohort 3 have been met.

Existing information on the registered substance itself derived from available *in vivo* studies [an oral 90-day study in rat [redacted] and a reproductive screening study in rat [redacted] show evidence of specific findings indicating a particular concern for developmental immunotoxicity. Specifically, the 90-day study shows lower relative and absolute thymus and spleen weights at 100 mg/kg/day in males. There is histopathological evidence of foamy macrophages in mesenteric lymph nodes (male and female), and the mesenteric lymph nodes additionally show pigmented macrophage foci in both sexes. You considered these histopathological effects in lymph nodes to be adverse. The reproductive screening study shows lymphoid atrophy in females at 100 mg/kg and there are macrophage foci in mesenteric lymph nodes in both sexes. There is additional supportive evidence of immune system activation by the registered substance. Specifically, in the 90-day study there is histopathological evidence of foamy macrophages in lung alveoli (females), small intestine lamina propria (male and female) and kidney glomeruli (male and female). In the reproductive screening study, there are foamy macrophages in ileum in both sexes.

In your comments on the PfA, you comment in respect of (1) thymus and spleen, and (2) foamy macrophages.

(1) Thymus and spleen: You argue that (i) the reported effects are marginal and non-specific (ii) the factual basis of the decision is wrong and (iii) the lower thymus and spleen weights are related to lower body weight and stress and suggestive for specific immunotoxicity.

(2) Foamy macrophages: (i) You propose various possible explanations for the foamy macrophages, and hypothesise about the mode of action and phospholipidosis. (ii) You note that related substances do not produce effects in developmental or reproduction studies. (iii) You state that "In conclusion, there is no relation between foamy macrophages, even when accompanied by signs of inflammation (increased neutrophils, and granulomatosis of tissues), and possible developmental disturbances."

ECHA addresses your comments as following:

(1) *Thymus and spleen:*
(i) ECHA relies upon effects on the weight of multiple organs which are statistically significant. While your dossier records for the OECD 422 study that there is "Thymus: increased incidence of lymphoid atrophy in females at 100 mg/kg/day", there is no results table provided. In your comment, you simultaneously contend that this study in fact shows "very marginal difference between the high dose (2 animals grade 1) and control (1 animal grade 1)" and that "Thymus: non-statistically significant reduced size at 300 mg/kg both males and females. Histopathology only mentions "Lymphoid atrophy - involution" observed in one control and 1 high dose female" (under a different heading for the OECD 422 study). ECHA cannot reconcile the differences between the above-mentioned statements included in your comments; nor the difference between these statements and the information included in the dossier as indicated above. As a result, ECHA relies upon the information included in the dossier for the purposes of the present decision making process. ECHA notes that the factual basis for considering that there is a concern for (developmental) immunotoxicity (e.g. the results set out in the 90-day study) is sufficient to justify that these findings are not merely marginal, even without the lymphoid atrophy findings. Although you contend that there may be a non-

specific basis for these findings, ECHA considers that you have not demonstrated that the basis for these findings is non-specific. (see also under (iii)).
(ii) ECHA accepts that there is no lymphoid atrophy in the 90-day study. ECHA notes that there are numerous discrepancies between the dossier and your comments (e.g. your comments state that the OECD 422 was at 300 mg/kg/day, the characterisation that there was lymphoid atrophy in the thymus (as opposed to reduced weight) in the 28-day study, that there were not significant effects on thymus or spleen weight in the 90-day study, all of which are in contradiction to the information in the dossier), and so ECHA relies upon the information in the dossier.
(iii) The 90-day study shows lower relative and absolute thymus and spleen weights at 100 mg/kg/day in males, and so this cannot be simply due to reduced body weight. You have not demonstrated that these effects are secondary to other toxicity, and so the particular concern for (developmental) immunotoxicity remains.

(2) *Foamy macrophages:*
(i) you hypothesise about the mode of action, but you have not demonstrated that these effects raise no particular concern for (developmental) immunotoxicity.
(ii) ECHA considers that you are making a read-across to structurally-related substances to conclude that there are no relevant effecs. The read-across to properties of other cationic surfactants is not justified according to Annex XI, 1.5, and this read-across is therefore unreliable. Further, the indicated studies from structurally-analogous substances (developmental toxicity studies, OECD 422, 2-generation reproductive toxicity studies) would not provide the information that the EOGRTS with DIT cohort would give.
(iii) ECHA considers that histopathological perturbation of an immune system cell to a level which is adverse gives rise to a concern for immunotoxicity. The supporting histopathological characterisation of foamy macrophages supports the concern for immune system perturbation.

ECHA considers that immunotoxicity and immune system perturbation observed in adults may trigger developmental immunotoxicity cohorts in an extended one-generation reproductive toxicity study unless substance specific information is provided why these effects or mode of action would not be relevant in a developing organism. In summary, ECHA concludes that you have not excluded that there are relevant triggers which give rise to a particular concern for (developmental) immunotoxicity.

Therefore, based on the results from the above-identified *in vivo* studies on the registered substance, ECHA concludes that the developmental immunotoxicity Cohort 3 needs to be conducted.

Species and route selection

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

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

c) Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Extended one-generation reproductive toxicity study (test method OECD TG 443), in rats, oral route, according to the following study-design specifications:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce systemic toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation; and
- Cohort 3 (Developmental immunotoxicity).

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

Notes for your consideration

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

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

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

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

Column 2 of Annex VII, Section 9.1.2 specifies that the study does not need to be conducted if there are mitigating factors indicating that aquatic toxicity is unlikely to occur for instance if the substance is highly insoluble in water or the substance is unlikely to cross biological membranes.

In the technical dossier you have provided a study record for a Growth inhibition to aquatic plants (OECD TG 201, [redacted] 2010). However, this study does not provide the information required by Annex VII, Section 9.1.2., because it is not adequate.

ECHA notes that your reporting of the effects identified is based on nominal concentrations instead of measured concentrations although the recovery concentration has been below 80%. This does not provide sufficient information to enable the relevance of the test to be assessed.

More explicitly, in the dossier, you provided the EC10 based on nominal concentrations, although analytical measurements have been done in the same study and significant loss from the water has been observed: "*The measured concentrations at test start were in the range of 79 – 89 % of the nominal values. At the end of the test Tall oil diethylenetriamine imidazoline was analysed at concentration levels 0.320 and 3.20 mg/L (prepared without algae) and gave recoveries of < LOQ - 22 % of the nominal values.*"

You further provide a justification *for the decreased recoveries: "Biodegradation as possible reason for this decrease is very unlikely considering the short time frame, also the river water was frozen before use to minimize the microbial activity. The decrease is attributed to additional sorption to suspended matter and DOC due to thermodynamically driven redistribution of the sorbed fraction. (...) Less than 1.6 % of the nominal concentration was observed sorbed to glassware. Therefore all effect values are given based on nominal concentrations of the test item."*

While ECHA may agree with your statement that the decrease in the recovery of the test material is unlikely to be due to biodegradation and that the registered substance does not seem to significantly adsorb on the glassware, the registered material seems to "*sorp to suspended matter and DOC*", and as a consequence, the test organisms would not be fully exposed to substance during the test.

ECHA notes that for adsorbing substances, effect concentrations should be expressed based on measured values (OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 ; ECHA *Guidance on information requirements and chemical safety assessment* (v.4.0, June 2017), Chapter R7b, Table R.7.8-3 and Appendix R.7.8-1).

Moreover, in the technical dossier you state that the "*long-term aquatic ecotoxicity tests with amidoamines/imidazolines were therefore performed in natural river water to allow a PECaquatic bulk/PNECaquatic bulk approach. and are considered to be conservative but more environmentally realistic than the standard method. This approach is based on PEC estimations representing 'total aquatic concentrations'. To characterize the risk to the aquatic compartment the PECaquatic, bulk is compared with the PNECaquatic, bulk derived from river water ecotoxicity studies*"

ECHA points out that assessment of PBT/vPvB shall be based on data obtained under relevant conditions (Annex XIII), and that "relevant conditions" means those conditions that allow for an objective assessment of the PBT/vPvB properties and not properties of a substance in particular environmental conditions. ECHA's Board of Appeal has confirmed this in its decision of 7 December 2016 in case A-013-2014.

ECHA further notes that OECD test guideline 201 recommends the use of standardised test media which do not contain suspended matter or dissolved organic carbon.

ECHA also notes that the technical dossier includes one wide-spread offshore use in oilfield formulations (ERC4). Furthermore, ECHA notes that the marine suspended matter concentration and DOC are much lower than the concentrations used in the algae ecotoxicity test (i.e. susp matter concentration of 16.2 mg/L and 3.9 mg/L DOC are reported in the technical dossier). Therefore, for the purpose of risk assessment, this approach overestimates the adsorption in the marine environment. Contrary to your statement, ECHA considers that your approach is not conservative for the marine environment, and therefore ECHA finds it inadequate for risk assessment purposes.

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.

Based on all the above, ECHA does not consider adequate the provided information to fulfil the REACH standard information requirement for the purpose of PBT/vPvB assessment.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you proposed to use the so-called 'bulk approach' for the environmental risk assessment. This approach would consist of comparing $PEC_{aquatic,\ bulk}$, representing the predicted concentration in environmental water containing dissolved organic carbon and suspended matter, to $PNEC_{aquatic,\ bulk}$ derived from river water ecotoxicity studies.

You justified this approach by stating that it would avoid the need for using the equilibrium partitioning method (EPM) in the risk assessment. You claimed that EPM was questionable for cationic surfactants.

You show an intention to use the results of the provided ecotoxicity study based on analytically measured concentration, for the seawater risk assessment, and for the CLP and PBT assessments. ECHA may agree with your intention if the dissolved organic carbon content falls within the guideline recommendations for the test medium (i.e. no added DOC, DOM or suspended matter).

ECHA further notes that deviating from the guideline by using river water (containing a higher TOC content and (potential) higher number of binding sites than the medium recommended in OECD TG 201 or 211) is not acceptable as it will underestimate the intrinsic toxicity of the substance to algae and to freshwater invertebrates.

Due to its physicochemical properties, the registered substance will tend to bind to any dissolved organic matter (DOM) and dissolved organic carbon (DOC) added to the test medium. Hence, when measuring the "dissolved" fraction from the test medium (i.e. generally defined as passing through a filter with a fine enough mesh, usually 0.45 µm), the substance bound to the DOM or to the DOC will be quantified together with the free substance. Only the free substance is deemed to cause toxicity. If this is the case, the measured values including not only the free subsance but also the fraction bound to DOM and DOC would underestimate the intrinsic toxicity of the registered substance.

Regarding the use of the EPM for cationic surfactants, ECHA agrees that it could be unreliable if partitioning between the solid phase and the aqueous phase is only based on hydrophobicity

(log Kow) or adsoption to organic carbon. For ionic substances in general, and for cationic surfactants in particular, adsorption/desorption can be indeed driven by other interactions. However, if experimentally measured adsorption/desorption values (Kd) are used instead of log Kow or Koc, then EPM could still be applied for the exposure assessment. You can use the Kd value obtained from the experimental OECD TG 106 study, already included in your technical dossier. You yourself supported the use of EPM with Kd in your comments to long-term sediment testing (see below, section 7 of the present decision).

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

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: Algae growth inhibition test, EU C.3./OECD TG 201) using the standard test media (i.e. without added DOC/DOM or suspended matter).

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

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

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

In the technical dossier you have provided a study record for a Long term toxicity to aquatic invertebrates (OECD TG 211; [redacted], 2010). However, this study does not provide the information required by Annex IX, Section 9.1.5., because it is not adequate.

ECHA notes that your reporting of the effects identified is based on nominal concentrations instead of measured concentrations although the recovery concentration has been below 80%. This does not provide sufficient information to enable the relevance of the test to be assessed.

More explicitly, in the dossier, the resulting NOEC and EC10 values were provided in nominal concentrations, although analytical measurements have been done in the same study and significant loss from the water has been observed: *"The recoveries in the fresh media were in the range of 73 to 86 % of the nominal values.In the old media (after 48 h or 72 h) the recoveries decreased to values in the range of 38 to 60 %."*

You provided a justification for the decreased recoveries: *"Biodegradation as possible reason for this decrease is very unlikely considering the short time frame, also the river water was frozen before use to minimize the microbial activity. The decrease is attributed to additional sorption to suspended matter and DOC due to thermodynamically driven redistribution of the sorbed fraction."*

You further include a statement that seem to contradict above findings: "*The results of the chemical analyses show that the test organisms were fully exposed to the test substance during the test. Therefore, all effect values given are based on the nominal test item concentrations.*"

While ECHA may agree with your statement that the decrease in the recovery of the test material is unlikely to be due to biodegradation and that the registered substance does not seem to significantly adsorb on the glassware, the registered material seems to "*sorp to suspended matter and DOC*", and as a consequence, the test organisms would not be fully exposed to substance during the test.

ECHA notes that for adsorbing substances, effect concentrations should be expressed based on measured values (OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 ; ECHA *Guidance on information requirements and chemical safety assessment* (v.4.0, June 2017), Chapter R7b, Table R.7.8-3 and Appendix R.7.8-1).

Moreover, in the technical dossier you state that the "*long-term aquatic ecotoxicity tests with amidoamines/imidazolines were therefore performed in natural river water to allow a PECaquatic bulk/PNECaquatic bulk approach. and are considered to be conservative but more environmentally realistic than the standard method. This approach is based on PEC estimations representing 'total aquatic concentrations'. To characterize the risk to the aquatic compartment the PECaquatic, bulk is compared with the PNECaquatic, bulk derived from river water ecotoxicity studies*"

ECHA points out that assessment of PBT/vPvB shall be based on data obtained under relevant conditions (Annex XIII), and that "relevant conditions" means those conditions that allow for an objective assessment of the PBT/vPvB properties and not properties of a substance in particular environmental conditions. ECHA's Board of Appeal has confirmed this in its decision of 7 December 2016 in case A-013-2014.

ECHA further notes that OECD test guideline 211 recommends that TOC levels in the medium (i.e. before addition of the algae) are below 2 mg/L.

ECHA also notes that the technical dossier includes one wide-spread offshore use in oilfield formulations (ERC4). Furthermore, ECHA notes that the marine suspended matter concentration and DOC are much lower than the concentrations used in the long-term toxicity to Daphnia ecotoxicity test (i.e. susp matter concentration of 16.2 mg/L and 3.9 mg/L DOC are reported in the technical dossier). Therefore, for the purpose of risk assessment, this approach overestimates the adsorption in the marine environment. Contrary to your statement, ECHA considers that your approach is not conservative for the marine environment, and therefore ECHA finds it inadequate for risk assessment purposes.

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.

Based on all the above, ECHA does not consider adequate the provided information to fulfil the REACH standard information requirement for the purpose of PBT/vPvB assessment.

You provided comments on the draft decision according to Article 50(1) of the REACH Regulation for this endpoint, together with Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.). Please see Section 3 for ECHA's response.

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

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) using the standard test media (i.e. without added DOC/DOM or suspended matter).

Notes for your consideration for for Sections 3 and 4

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

Due to the adsorbing properties of the registered substance you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6/REV1 (6 July 2018) and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

5. Sediment simulation testing (Annex IX, Section 9.2.1.4.)

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

"Sediment simulation testing" is a standard information requirement as laid down in Annex IX, section 9.2.1.4. of the REACH Regulation for substances with a high potential for adsorption to sediment.

The registered substance is surface active and is highly adsorptive (Kod: 47249). Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement Annex XI, Section 3.2.(ii). You provided the following justification for the adaptation: "*The Predicted no effect concentration for the benthic compartment will be calculated applying the equilibrium partitioning method. Due to the high observed sorption to soil an additional factor of 10 will be applied to compensate for additional exposure via ingestion.*"

However, ECHA notes that your adaptation does not meet the general rule for adaptation of Annex XI, Section 3.2.(ii). ECHA *Guidance on information requirements and chemical safety*

assessment (v.4.0, June 2017), Chapter R7b states that "*EPM is based on sorption to organic matter. Therefore, it cannot be used for some classes of substances, e.g. when binding behaviour is not driven by lipophilicity (e.g. aromatic amines forming covalent bonds to sediment components, ionisable substances, surface active substances)*." Thus, the provided adaptation arguments are not sufficiently justified.

According to Annex IX, Section 9.2.1.4, column 2 of the REACH Regulation, simulation testing on sediment does not need to be conducted if the substance is readily biodegradable or if direct or indirect exposure of sediment is unlikely.

ECHA notes that based on the information in the technical dossier, and the provided endpoint summary at Biodegradation in water: screening tests, the registered substance is not readily biodegradable in several OECD 301C and D tests and you conclude it as being *inherently biodegradable*.

Regarding exposure of sediment, the substance is surface active and it is highly adsorptive (Kd: 47249). Furthermore, based on the uses reported in the technical dossier, ECHA considers that sediment exposure cannot be excluded (*e.g.* offshore use in oilfield formulations in closed systems (corrosion inhibitors) use reported, to which ERC 4 use descriptor was assigned). ECHA therefore considers that you have not demonstrated that sediment exposure is unlikely.

ECHA notes that in order to conclude that a substance is not P, you should demonstrate that the substance will not persist in any of the environmental compartment, i.e. not P in water, not P in sediment, not P in soil. It looks like the substance can hydrolyse. However, hydrolysis may be in competition with adsorption in sediment (and in soil, the substance is highly adsorptive (Kd: 47249)), which could limit or inhibit the hydrolysis reaction.

Therefore, degradation in sediment (or soil) is likely to be slower than in water, and therefore a simulation test in sediment (or in soil) can be regarded as a worst-case: if the substance is shown to be not P in sediment or in soil, then it will likely not be P in water and you may not need to conduct further tests. According to the reported uses of the substance, a test in sediment seems to be more relevant than a test in soil.

ECHA notes also that you have not provided adequate justification in your chemical safety assessment (CSA) or in the technical dossier for why there is no need to investigate further the degradation half-life of the substance and its degradation products. As explained further below, ECHA considers that the information is needed for the PBT/vPvB assessment.

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

In your comments on the draft decision according to Article 50(1) of the REACH Regulation you have stated that, despite of the challenges you may encounter in the testing, you agree to perform the requested test.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.
According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Aerobic and anaerobic transformation in aquatic

sediment systems (test method EU C.24. / OECD TG 308) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.4.

One of the purposes of the simulation test is to provide the information that must beconsidered for assessing the P/vP properties of the registered substance in accordance with Annex XIII of REACH Regulation to decide whether it is persistent in the environment. Annex XIII also indicates that "*the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions*". The Guidance on information requirements and chemical safety assessment R.7b (version 4.0, June 2017) specifies that simulation tests "attempt to simulate degradation in a specific environment by use of indigenous biomass, media, relevant solids [...], and a typical temperature that represents the particular environment". The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-8 (version 3.0 February 2016) indicates 12°C (285K) as the average environmental temperature for the EU to be used in the chemical safety assessment. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD TG 308. Therefore, the test should be performed at the temperature of 12°C.

Simulation tests performed in sediment or in soil possibly imply the formation of non-extractable residues (NER). These residues (of the parent substance and/or transformation products) are bound to the soil or to the sediment particles. NERs may potentially be re-mobilised as parent substance or transformation product unless they are irreversibly bound or incorporated into the biomass.

When reporting the non-extractable residues (NER) in your test results you should explain and scientifically justify the extraction procedure and solvent used obtaining a quantitative measure of NER.

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: Aerobic and anaerobic transformation in aquatic sediment systems (test method: EU C.24./OECD TG 308). The biodegradation of each relevant constituent present in concentration at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study.

Notes for your consideration

Before conducting the requested test you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment, Chapter R7b, Sections R.7.9.4 and R.7.9.6 (version 4.0, June 2017) and Chapter R.11, Section R.11.4.1.1 (version 3.0, June 2017) on PBT assessment.

In accordance with Annex I, Section 4, of the REACH Regulation you should revise the PBT assessment when results of the test detailed above is available. You are also advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 3.0, June 2017), Chapter R.11, Section R.11.4.1.1. and Figure R. 11-3 on PBT assessment for the integrated testing strategy for persistency assessment in particular taking into account the degradation products of the registered substance.

6. Identification of degradation products (Annex IX, Section 9.2.3.)

The identification of the degradation products is a standard information requirement according to column 1, Section 9.2.3. of Annex IX 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.

One of the Member State Competent Authorities submitted a proposal for amendment to add a request for the identification of degradation products (Annex IX, 9.2.3.).

According to Annex IX, Section 9.2.3., column 2 of the REACH Regulation, identification of degradation products is not needed if the substance is readily biodegradable. ECHA notes that based on the information in the technical dossier, the registered substance is not readily biodegradable as also discussed in section 5. above.

You have not provided any information on the degradation products of the registered substance. The technical dossier does also not contain an adaptation in accordance with column 2 of Annex IX, Sections 9.2 or 9.2.3. or with the general rules of Annex XI for this standard information requirement.

Furthermore, ECHA notes that you have not provided any justification in your chemical safety assessment (CSA) or in the technical dossier for why there is no need to provide further information on the degradation products. ECHA considers that this information is needed in relation to the PBT/vPvB assessment and risk assessment.

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

Regarding appropriate and suitable test method, the methods will have to be substance-specific. When analytically possible, identification, stability, behaviour, molar quantity of metabolites relative to the parent compound should be evaluated. In addition, degradation half-life, log Kow and potential toxicity of the metabolite may be investigated. You may obtain this information from the simulation study requested in this decision (request 5), or by some other measure. You will need to provide a scientifically valid justification for the chosen method.

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:

Identification of the degradation products (Annex IX, Section 9.2.3.) by using an appropriate and suitable test method, as explained above in this section.

Notes for your consideration

Before providing the above information you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R.7b., Sections R.7.9.2.3 and R.7.9.4. These guidance documents explain that the data on degradation products is only required if information on the degradation products following primary degradation is required in order to complete the chemical safety assessment. Section R.7.9.4. further states that when substance is not fully degraded or mineralised, degradation products may be determined by chemical analysis.

7. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.)

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

"Bioaccumulation in aquatic species, preferably fish" is a standard information requirement as laid down in Annex IX, Section 9.3.2.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 XI, Section 1.3. You provided a QSAR performed with the BCFBAF v3.01 programme (Episuite, 2010), with a provided reliability of 2: *"BCF estimated using a measured Log Kow value"*. You further explain in the technical dossier: *"APPLICABILITY DOMAIN: Applicability to surface active agents not documented."*

However, ECHA notes that your adaptation does not meet the specific rule for adaptation of Annex XI, Section 1.3. because the BCFBAF v3.01 dataset does not include surface active substances. Therefore, surface active substances are outside the applicabiliy domain, and thus, the prediction is not reliable.

In the CSR, you further state: *"Standard OECD 305 tests are technically not feasible with these strongly sorbing hydrolytically unstable substances. In addition is the route of exposure in an standard OECD 305 test unrealistic for these substances because the substance will either be sorbed or (bio)degraded. The bioaccumulation potential of the alkyl amidoamines/imidazolines was therefore assessed based on a measured log Kow.*
As indicated before, alkyl amidoamines/imidazolines are hydrolyzed and consequently biodegraded and it is therefore unlikely that they will accumulate in the food chain. Since there is a log Kow measured using the slow-stirring method according to OECD 123, this value is used to assess the bioaccumulation potential."

You further explain that *"Despite the fact that the log Kow is measured applying the most appropriate method according to the REACH guidance i.e. the slow stirring method (OECD 123), there is unfortunately no reliable relationship between the measured log Kow and BCF for this type of substances."*

ECHA notes that for some groups of substances, such as surface active substances, log Kow is not a valid descriptor for assessing the bioaccumulation potential. Information on bioaccumulation of such substances should therefore take account of other descriptors or mechanisms than hydrophobicity (ECHA Guidance on information requirements and chemical safety assessment, Chapter R.11, Section R.11.4.1.2.10; version 3.0, June 2017).

Furthermore, you state that the *"OECD 305 tests are technically not feasible with these strongly sorbing hydrolytically unstable substances"*. The OECD 305 TG (2012) explains that *"for highly hydrophobic substances the dietary test is recommended"*. Moreover, it states *"for surfactants it should be considered whether the aqueous bioconcentration test is feasible, given the substance properties, otherwise the dietary study is probably more appropriate."*

Thus, ECHA notes that given the adsorptive properties of the registered substance, the oral route is the relevant exposure route. Furthermore, the OECD TG 305 discusses the possible need to perform dietary exposure test when testing surface active substances (paragraph 12). Although it also mentioned (paragraph 14) that "*approaches are available to estimate a kinetic bioconcentration factor (BCF_K) from data generated in the dietary study (..). In general, these approaches assume first order kinetics, and are only applicable to certain groups of compounds. It is unlikely that such approaches can be applied for surfactants*".

No criteria (cut off value) are established in Annex XIII of REACH for the BMF values determined in the dietary test. However, it is indicated in chapter R.11.4.1.2.9 of the PBT guidance, that a depuration rate (k2) calculated from a dietary study can be used as such to identify substances with a high potential for bioaccumulation. It is worth noting that in the context of SVHC identification, depuration rate k2 has been used as main element to conclude that a substance was very bioaccumulative.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you have stated that OECD 305-III is not applicable to the registered substance, as actually mentioned on paragraph 15 of the guideline: "*It is unlikely that such approaches* [which convert BMF into BCFk] *can be applied for surfactants*", and you propose OECD 305 TG request to be removed from the present decision.

As addressed above, the OECD TG 305 oral route is the relevant exposure route for this substance. You must attempt to estimate the corresponding BCF value from the dietary test (OECD 305-III) data according to Annex 8 of the OECD 305 TG and OECD Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation, ENV/JM/MONO (2017)16. In any case you must report all data derived from the dietary test as listed in the OECD TG 305-III. The depuration rate has been previously used to identify bioaccumulation potential, and cationic surfactants should not be an exception.

Concerning the need to perform the test, an integrated testing strategy (ITS) approach applies, as explained below under "Notes for your consideration". According to this ITS, if the substance and all its constituents and degradation products are observed to be non- P/vP, then you could waive the test on bioaccumulation.

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

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7c* (version 3.0, June 2017) bioaccumulation in fish: aqueous and dietary exposure (test method EU C.13. / OECD TG 305) is the preferred test to cover the standard information requirement of Annex IX, Section 9.3.2.

ECHA Guidance defines further that results obtained from a test with aqueous exposure can be used directly for comparison with the B and vB criteria of Annex XIII of REACH Regulation and can be used for hazard classification and risk assessment. Comparing the results of a dietary study with the REACH Annex XIII B and vB criteria is more complex and has higher uncertainty. Therefore, the aqueous route of exposure is usually the preferred route and shall be used whenever technically feasible. However, in this specific case, due to the

physicochemical properties of the registered substance the most relevant test is the dietary exposure route. Therefore, you shall attempt to estimate the corresponding BCF value from the dietary test data by using the approaches given in Annex 8 of the OECD 305 TG. In any case you shall report all data derived from the dietary test as listed in the OECD 305 TG in your robust study summary.

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 Bioaccumulation in fish: dietary exposure bioaccumulation fish test (test method: OECD TG 305-III). The bioaccumulation of each relevant constituent present in concentration at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study.

Notes for your consideration

Before conducting the above test you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, June 2017), Chapter R.11.4. and Figure R.11-4 on the PBT assessment for further information on the integrated testing strategy for the bioaccumulation assessment of the registered substance. In particular, you are advised to first conclude whether the registered substance may fulfil the REACH Annex XIII criteria of being persistent or very persistent, and then to consult the PBT assessment for Weight-of-Evidence determination and integrated testing strategy for bioaccumulation assessment. You should revise the PBT assessment when information on bioaccumulation is available.

8. Long-term toxicity to sediment organisms (Annex X, Section 9.5.1.)

"Long-term toxicity to sediment organisms" is a standard information requirement as laid down in Annex X, Section 9.5.1. 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.

ECHA notes that you have sought to adapt the long-term toxicity testing on sediment organisms using the following justification: "*The Predicted no effect concentration for the benthic compartment will be calculated applying the equilibrium partitioning method. Due to the high observed sorption to soil an additional factor of 10 will be applied to compensate for additional exposure via ingestion.*"

ECHA notes that in order for an adaptation of Annex X, 9.5.1. Column 1 provisions to be justified, you would have to demonstrate by means of the Chemical Safety Report (CSR) that the conditions of an adaptation possibility (Annex XI) are fulfilled. In establishing this, in some cases and as explained in ECHA Guidance on information requirements and chemical safety assessment (R.7b, version 4.0, June 2017, Section R.7.8.7.), you may use the EPM as part of a weight-of-evidence to adapt the standard information requirement.

However, according to ECHA Guidance on information requirements and chemical safety assessment (R.7b, version 4.0, June 2017, Section R.7.8.10.1.) the *EPM cannot be used for some classes of substances, e.g. when binding behaviour is not driven by lipophilicity (e.g.aromatic amines forming covalent bonds to sediment components, ionisable substances, surface active substances)*. For such substances at least one sediment study has to be performed. ECHA notes that the registered substance has a reported surface activity of 34

mN/m (i.e. it has surface activity), thus ECHA considers that long-term sediment testing is indicated for the registered substance.

ECHA notes that you have not demonstrated that available data would lead to the conclusion that the substance is or is not toxic to sediment organisms (Annex XI, 1.2.). In fact, the present substance has a high potential to adsorb to sediment. Therefore, as the standard information requirements for long-term sediment testing have not been adapted in a justified manner, testing is required.

Therefore, in this specific case, you have not justified an adaptation.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you proposed to use EPM to predict the hazards for the benthic compartment. To this end, you proposed to use Kd instead of Koc in the EPM approach.

You compared observed vs. predicted NOEC/EC10 from 8 cationic substances based on data from long-term Daphnia and benthic organisms, and concluded that for 5 out of 8 substances this ratio was higher than 1 without applying the additional factor of 10 for additional exposure via ingestion for strongly sorbing substances.

ECHA reminds you that the use of EPM for the hazard assessment is based on the following assumptions (ECHA *Guidance on information requirements and chemical safety assessment* R.7b, v.4.0 June 2017):

- The concentration of contaminant adsorbed on the solid phase and the concentration of contaminant dissolved in the pore water are in equilibrium and can be predicted from each other using an appropriate partitioning coefficient. As discussed above, a partitioning coefficient based only on log Kow or Koc would not be appropriate for cationic surfactants. However, ECHA agrees that a Kd value could be used instead (see also section 3 of the present decision).

- Only the substance dissolved in the pore water is regarded as bioavailable. It implies that EPM may only be seen as an appropriate surrogate for organisms that are exposed exclusively to the sediment pore water and that have a water permeable epidermis. However, other exposure routes are possible. For example, oligochaetes feed on solid particles, and a significant amount of contaminant may affect them via the oral route. To this end, an additional safety factor of 10 has to be applied when calculating the PEC/PNEC ratio for highly adsorptive or binding substances in order to take into account the additional uncertainties due to potential intake through direct ingestion of particles. ECHA notes that in your comparison between experimental benthic toxicity vs results predicted by EPM, EPM could be concluded to be more conservative in 3 cases out of 8 only because an extra safety factor of 10 was applied.

- The intrinsic sensitivity of benthic organisms is assumed to be the same as the intrinsic sensitivity of pelagic organisms. The actual sensitivity of benthic organisms depend on many factors such as their morphology and physiology, life-span, feeding behaviour and characteristics of their digestive system, etc.

Your comparison between experimental benthic toxicity vs. results predicted by EPM lacks the minimum information for ECHA to be able to assess its validity and reliability (ECHA *Guidance on information requirements and chemical safety assessment* R.7b, v.4.0 June 2017 and R.6, May 2008), e.g.:

- the quality/reliability of the test methods, test media, tested benthic organism species and study records *per se* cannot be analysed since they are not included
- the used test materials (impurities, constituents etc) are unknown
- the boundaries of the extrapolation are not provided: are these 8 substances representative of the registered substance?

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Sediment-water Chironomid toxicity using spiked sediment (Test method: OECD TG 218) or Sediment-water Lumbriculus toxicity test using spiked sediment (Test method: OECD TG 225) or Sediment-Water Chironomid Life-Cycle Toxicity Test Using Spiked Sediment (OECD TG 233).

Notes for your consideration

The Sediment-water Chironomid toxicity using spiked sediment (OECD TG 218), Sediment-water Lumbriculus toxicity test using spiked sediment (OECD TG 225) and Sediment-Water Chironomid Life-Cycle Toxicity Test Using Spiked Sediment (OECD TG 233) are in principle each considered capable of generating information appropriate for the fulfilment of the information requirements for sediment long-term toxicity testing. ECHA is not in a position to determine the most appropriate test protocol, since this decision is dependent upon species sensitivity, substance properties and uses. ECHA considers that it is your responsibility to choose the most appropriate test protocol and to give a justification for the choice. You may carry out more than one of the sediment tests defined in Section II above if you consider that further testing is required. While ECHA at this stage only requires one test, based on newly available data it may consider whether further tests are required to fulfil the standard information requirement.

9. Identification of PNEC and risk characterisation (Annex I, Sections 3.3.1. and 6.)

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

Annex I, Section 3.1.5. of the REACH Regulation requires that the study or studies giving rise to the highest concern shall normally be used to draw a conclusion and a robust study summary shall be prepared for that study or studies and included in the technical dossier. In addition, Annex I, Section 3.1.5. requires that if a study giving rise to the highest concern is not used, then this shall be fully justified.

You have provided the following key study summaries for tests on short-term fish and aquatic invertebrates toxicity, as well as for toxicity on long-term aquatic invertebrates and growth inhibition tests on aquatic plants:

a. Short-term toxicity to fish test (OECD TG 203): [redacted] (2009) reliability 1, providing a 96h-LC50 of 0.19 mg/L, measured concentration, with *Danio rerio* on filtered water.
b. Short-term toxicity to aquatic invertebrate test (OECD TG 202): [redacted] (2009) reliability 1, providing a 48h-EC50 of 0.18 mg/L, measured concentration on filtered

water.

c. Long-term toxicity to aquatic invertebrate test (OECD TG 211): [redacted] (2010) reliability 1, providing a 21d-EC10 of 0.255 mg/L nominal concentration of active ingredients, on natural river water with suspended matter concentration of 16.2 mg/L and 3.9 mg/L DOC.
d. Alga growth inhibition test (OECD TG 201): [redacted] (2010) reliability 1, providing a 72h-EC10 of 0.343 mg/L nominal concentration of active ingredients with *Pseudokirchneriella subcapitata*, on natural river water with suspended matter concentration of 16.2 mg/L and 3.9 mg/L DOC.

You have used the results from the Long-term toxicity to aquatic invertebrate key study to derive PNEC sediment and PNEC soil by applying the equilibrium partitioning method (EPM) with an additional factor of 10.

ECHA notes that the technical dossier includes data from short-term toxicity tests on fish and Daphnia performed on filtered water, where the effect values are provided on measured data. Provided that the effect concentrations on algae are not regarded as adequate for the CSA (see request 3 above). Therefore, currently valid information on a short term test performed on a third species is missing to be able to derive the PNECs.

Besides, ECHA would like to note in cases where the acutely most sensitive species has an L(E)C50 value lower than the lowest long term result (e.g. EC10 or NOECs) value, PNEC can be derived by using an assessment factor of 100 to the lowest L(E)C50 of the short-term tests (ECHA *Guidance on information requirements and chemical safety assessment* R.10, Table R.10-7, May 2008).

On the other hand, you have chosen to apply the Equilibrium Paritioning Method (EPM) for PNEC sediment and PNEC soil derivation. However, the technical dossier states that the registered substance is a cationic surfactant and has a high adsorption coefficient (Log Koc: 5.98).

According to ECHA *Guidance on information requirements and chemical safety assessment* (R.7b, version 4.0, June 2017, Section R.7.8.7.) the EPM cannot be used in a weight of evidence approach for substances that are surface active. For such substances at least one sediment study has to be performed.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation you agreed to provide an updated effect and risk assessment.

You proposed to provide PNECmarine-water based on revised measured concentrations, the PNEC freshwater based on nominal concentrations –following the bulk approach-, PNECsediment based on EPM, and that you have already provided a PNEC soil calculated on the basis of the availability of one long term earthworm test.

You further argue the possibility of using Kd instead of Koc at EPM approach, which ECHA agrees to for the exposure assessment. However, as discussed above, ECHA does not agree on the validity of the use of EPM approach for assessing the sensitivity of benthic organisms, nor the use of the bulk approach for the risk assessment.

The effect concentrations on algae, at least, are not regarded as adequate for the CSA (see request on growth inhibition study on aquatic plant (request No.3) sabove). Therefore,

currently valid information on three short-term tests performed on three trophical levels is missing. This information is required to be able to derive the PNEC (ECHA *Guidance on information requirements and chemical safety assessment* R.10., Section R.10.3., May 2008).

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to revise PNECs for freshwater, marine water, intermittent releases, freshwater sediment and marine sediment:

- using the study giving rise to the highest concern (currently, for PNECaquatic short-term toxicity to aquatic invertebrates, [redacted] 2009) according to Annex I, Section 3.1.5 and revise the risk characterisation accordingly *or* provide a full justification for not using the study giving rise to the highest concern;
- using the default assessment factors and other recommendations of ECHA Guidance R.10 and revise the risk characterisation accordingly *or* provide a detailed justification on how the chosen approach meets the general requirements for PNEC derivation as described in Section 3.3. of Annex I, if not using the recommendations of ECHA Guidance R.10 for PNEC derivation.

Notes for your consideration

The results of the studies based on measured concentrations as requested under Appendix 1, Section 3 above shall be taken into account when revising the PNECs.

In order to derive PNECsediment, you should consider whether there is a need to investigate further the effects on sediment organisms, and if necessary, submit testing proposals for additional a long-term sediment test. The same applies for PNEC soil derivation.

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

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

If the substance fulfils the criteria for any of the hazard classes or categories listed in Article 14(4) of the REACH Regulation, the chemical safety assessment must include exposure assessment (including exposure scenarios) and exposure estimation (Annex I, Section 5), as well as risk characterisation (Annex I, Section 6).

In the present case, your registered substance is classified as a skin sensitiser, cat 1A (H317) and skin corrosive, cat. 1C (H314), as well as aquatic acute, cat. 1 (H400) and aquatic chronic, cat. 1 (H410). These are all hazard categories listed in Article 14(4) of the REACH Regulation triggering the need for exposure assessment as mentioned in the paragraph above.

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. Emission estimation shall be performed under the assumption that the risk management measures (RMMs) and operational conditions (OCs) described in the exposure scenario (ES) have been implemented. These RMMs and OCs should be included in the ESs provided in a CSR.

According to the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.16 (version 3.0, February 2016) the exposure scenario should contain information about OCs and RMMs based on which the assumed release factors and daily use rates can be justified. In a first instance, or in the absence of more specific information, assessors may use the release factors associated to the Environmental Release Categories (ERCs) to carry out their release estimation. If a specific RMM is applied in current practice and the effectiveness of such a technique for the respective substance is known, and clearly addressed (REACH Regulation, Annex I, 5.2.4.), release factors can be reduced accordingly and taken into account in the development of the Exposure Scenarios. The Guidance indicates that sector specific environmental release categories (spERCs) developed by industrial sector organisations can be used in place of the conservative default ERCs of ECHA guidance. Detailed explanations on the origin of the release factors are to be provided in the CSR and the conditions of use are to be communicated via the exposure scenarios annexed to the safety data sheet (SDS). As far as possible, spERCs have to be linked to the applied RMM and OC driving the release estimation.

In the CSR you have provided four ESs: [redacted]

ECHA notes that, in order to cover any exposures that may be related to the identified hazards, exposure estimation for most of the ESs (except ES 1) as stated by you in the CSR should be based on default parameters to derive the environmental release rate (Table R.16-7 of the Appendix A.16-1 of the *Guidance on information requirements and chemical safety assessment* Chapter R.16 (version 3.0, February 2016)) or on sector specific environmental release category (spERC) release factors.

ECHA considers that an adequate and detailed justification (e.g. based on RMMs and/or OCs and/or substance properties) of release factors used in exposure estimation, other than the default ERC and spERC release factors, is not provided in the CSR (e.g. it is not clear the reason for using reduced release factors from spERC ESVOC SpERC 6.1.a. v1 and CHARM manual v.1.4 (feb 2005) used in exposure estimation). Where internal measurements of releases are available, the summary of results of these measurements is needed (e.g. ES 1). This summary should be detailed enough to understand whether or not it covers relevant scenarios for possible releases from processing the substance according to the relevant ES.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you agree to "*provide an updated exposure and risk assessment*".

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation you are requested to use default release factors of ECHA Guidance R.16 and/or specific spERC and revise the risk characterisation accordingly *or* provide a detailed justification (e.g. based on RMMs and/or OCs and/or substance properties) for not using the default release factors as recommended in ECHA Guidance R.16 and/or in specific spERC fact sheet for estimation of environmental exposure.

Notes for your consideration

The revised PNECs requested with this decision shall be taken into account when assessing the related risks.

11. 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.
If the substance fulfils the criteria for any of the hazard classes or categories listed in Article 14(4) of the REACH Regulation, the chemical safety assessment must include exposure assessment (including exposure scenarios) and exposure estimation (Annex I, Section 5), as well as risk characterisation (Annex I, Section 6).

As stated in the section above, your registered substance is classified as hazardous as listed in Article 14(4) 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."

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.

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. Some 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 with DNELs derived from repeated dose toxicity studies. However, a primary concern in the workplace is to ensure that the likelihood of effects (skin sensitisation and severe burns 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. Whilst some engineering controls to help prevent dermal exposure are included in your CSR, and you describe personal protective equipment, currently your CSR lacks information on administrative controls such as procedures and training to ensure that workers are protected from sensitisation effects of the registered substance.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you agree to "*provide an updated exposure and risk assessment*".

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 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.

ECHA
EUROPEAN CHEMICALS AGENCY

Appendix 2: Procedural history

ECHA notes that the tonnage band for several members of the joint submission is 1 000 tonnes or more per year (Submission number: [redacted] Submission date: 18 May 2018). ECHA will proceed with the current decision making process based on that submission. This is not affected by your comment that you intend to change your joint submission tonnage band from 1000 or more to 100 – 1000 tonnes per year in the future.

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 13 of August 2018.

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

ECHA notified you of the draft decision and invited you to provide comments within 30 days of the notification.

ECHA took into account your comments and did amend the request(s).

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

ECHA received proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments and 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.

In addition, you provided comments on the draft decision. These comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5).

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-66 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

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

2. We contact you in your capacity as lead registrant, on behalf of the Joint Submission

3. Failure to comply with the requests in this decision will result in a notification to the enforcement authorities of your Member State.

4. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

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

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