~~Confidential~~

Helsinki, 10 October 2022

Addressees
Registrants of JS-mono-204-690-6-59002 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
26/04/2017

Registered substance subject to this decision ("the Substance")
Substance name: Dodecylamine
EC number: 204-690-6

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***15 January 2027.***

Requested information must be generated using the Substance unless otherwise specified.

Information required from all the Registrants subject to Annex VII of REACH

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

2. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202)

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

4. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: EU C.4. C/D/E/F/OECD TG 301B/C/D/F or EU C.29./OECD TG 310)

Information required from all the Registrants subject to Annex VIII of REACH

5. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)

6. If negative results are obtained in test performed for the information requirement of Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

7. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD TG 203)

Information required from all the Registrants subject to Annex IX of REACH

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

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

   For reasons explained in section 9 of Appendix 1, the test sample must be chosen to minimise gastrointestinal irritation and to allow investigation of intrinsic properties at adequate dose levels. This could be achieved by testing a neutral salt of the Substance.

10. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)

11. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210)

12. Long-term toxicity on terrestrial invertebrates also requested below (triggered by Annex IX, Section 9.4.1., column 2)

13. Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: EU C.21./OECD TG 216 and test method: EU C.22./ OECD TG 217)

14. Long-term toxicity on terrestrial plants also requested below (triggered by Annex IX, Section 9.4.3., column 2)

Information required from all the Registrants subject to Annex X of REACH

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

    For reasons explained in section 9 of Appendix 1, the test sample must be chosen to minimise gastrointestinal irritation and to allow investigation of intrinsic properties at adequate dose levels. This could be achieved by testing a neutral salt of the Substance.

16. Long-term toxicity testing on terrestrial invertebrates (Annex X, Section 9.4.4.; test method: EU C.33/OECD TG 222 or EU C.32/OECD TG 220 or EU C.39/OECD TG 232)

17. Long-term toxicity on terrestrial plants (Annex X, Section 9.4.6.; test method: EU C.31/OECD TG 208 with at least six species tested or ISO 22030)

18. Long-term toxicity testing on sediment organisms (Annex X, Section 9.5.1.; test method: EU C.27/OECD TG 218 or EU C.35/OECD TG 225 or EU C.40/OECD TG 233 with spiked sediment or EU C.51/OECD TG 239 using spiked sediment)

The reasons for the decision(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and

their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

In the requests above, the same study has been requested under different Annexes. This is because some information requirements may be triggered at lower tonnage band(s). In such cases, only the reasons why the information requirement is triggered are provided for the lower tonnage band(s). For the highest tonnage band, the reasons why the standard information requirement is not met and the specification of the study design are provided. Only one study is to be conducted; all registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the others under Article 53 of REACH.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report, where** relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the decision
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
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[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons for the decision

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0. Reasons common to several requests

0.1. Assessment of the read-across approach

1 You have adapted the following standard information requirements by using grouping and read-across approach under Annex XI, Section 1.5:

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Pre-natal developmental toxicity study in a second species (Annex X, Section 8.7.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)
- Long-term toxicity testing on terrestrial invertebrates (Annex X, Section 9.4.4.)
- Long-term toxicity testing on terrestrial plants (Annex IX, Section 9.1.5.)
- Long-term toxicity testing on sediment organisms (Annex X, Section 9.5.1.)

2 ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following sections.

3 Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group.

4 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

5 You provide a read-across justification document in IUCLID Section 13.

0.1.1. Scope of the grouping of substances (category)

6 For the purpose of this decision, the following abbreviations are used for the category members:

C12	Dodecan-1-amine, EC No. 204-690-6;
C12-14	C12-14-(even numbered)-alkylamines
C12-18C18u	Amines, C12-18 (even numbered) and C18-(unsaturated)alkyl, EC No. 701-068-0
C16-18C18u	C16-18-(even numbered, C18-unsaturated)-alkylamines, EC No. 263-125-1
C16-18	C16-18-(even numbered)-alkylamines,EC No. 292-550-5
C16-18su	C16-18-(even numbered, saturated and unsaturated)-alkylamines, EC No. 627-034-4
C18	Octadecan-1-amine, EC No. 204-695-3.

7 You justify the grouping of the substances as: "*All substances share the basic structure of*

primary fatty amines (PFA) with even numbered single alkyl moieties ranging from C12 to C18. The molecular structure is characterized by the hydrophobic aliphatic alkyl chain as well as a hydrophilic amine group, which provide the whole molecule with amphiphilic properties. […] *PFA category members possess a positively charged cationic amine structure and are strong bases under relevant conditions.* […] *PFA category members are considered also biologically equivalent because they follow the same metabolic pathways of oxidation by monoamine oxidases to generate the respective fatty acid and ammonia. […]. A category-based approach for* "N-alkyl-(C8-C18)-primary amines and Acetate Salts" *was also used to establish the exemption from the requirement of a tolerance for residues of primary alkylamines and their respective acetate salts [EPA-HQ-OPP-2009-0046FRL-8836-4]* […], *a* "fatty nitrogen derived amines category" *was also established within EPA's HPV Challenge Program (EPA, 2010b) as well as by the German GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA, 1996).* […] *Finally, consistency between category members is established by QSAR predictions*".

8 You define the applicability domain as primary aliphatic amines with linear (i.e. not branched) alkyl chains consisting of even number of carbon atoms. The number of carbon atoms in the alkyl chain of the category members ranges between 12 and 18 (smaller fractions of shorter alkyl chains in mixtures with different chain lengths are tolerated). The alkyl chains are primarily saturated, but mono-unsaturated carbon chains are also within the applicability domain.

9 ECHA understands that this is the applicability domain of the grouping and your predictions are assessed on this basis.

0.1.2. Predictions for (eco)toxicological and fate properties

10 You predict the properties of the Substance from information obtained from the following source substances:

C12	dodecan-1-amine, EC No. 204-690-6 (CAS RN 124-22-1)
CC	amines, coco alkyl, EC No. 262-977-1 (CAS RN 61788-46-3)
OL	octadec-9-en-1-amine, EC No. 204-015-5 (CAS RN 112-90-3)
TA	amines, tallow alkyl, EC No. 263-125-1 (CAS RN 61790-33-8)
HT	amines, hydrogenated tallow alkyl, EC No. 262-976-6 (CAS RN 61788-45-2)
OD	octadecan-1-amine, EC No. 204-695-3 (CAS RN 124-30-1)

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

- "[…] *all category members share the primary hazard of producing strong local effects on the skin (irritation or corrosion) and indications regarding repeated dose toxicity*";
- "[…] *Within relevant profilers checking for structural and mechanistic consistency* [from the OECD QSAR Toolbox profiler], *no differences between the structures were identified* […]";
- You also state that the category members show consistent trends in terms of physico-chemical properties;
- "*Prominent in the toxicity profile of PFA category members is their strong local effect with category members being either corrosive or irritating to the skin* […]";
- "*No skin sensitization was observed in tests on two PFA category members spanning the carbon chain length spectrum from C12 to C18*";
- "*The profiling results of the QSAR Toolbox both for the uncharged and the protonated category constituents as well as analyses performed with DEREK Nexus show consistency among all PFA category members and do not provide alerts for these endpoints* […]" [i.e., reproduction and developmental toxicity studies];
- "*Regarding toxicokinetics, uptake and elimination are considered to be comparable for all PFA category members. This view is supported since several aliphatic amines are normal constituents of mammalian urine*";

- "*While short-chained aliphatic amines are relatively well-absorbed, increasing of the chain length to C6 and greater decreases absorption* […]";
- "[…] *independent of the chain length aliphatic amines are metabolized via the same pathways. […] According to general biochemical knowledge, the metabolism of unsaturated alkyl chains will be similar to saturated alkyl chains*".

12 You provide the following additional reasoning for the prediction of ecotoxicological properties:

- "*Overall, the data show comparable levels of toxicity to aquatic organisms without a clear trend within the category. The differences observed may be more related to questions of sorption and bioavailability than to differences between PFA category members"*;
- "[…] *the data for the aquatic toxicity of C18 PFA suggest a similar toxicity to daphnids and algae than the one observed for C12 and C12-18C18u PFA (when all data are considered)*";
- "*Overall, we conclude that a read-across of aquatic toxicity data from one category member to another category member is scientifically justified. This interpretation is supported by the identical classification of all seven compounds, five of which have a harmonised classification*";
- "*Overall, the data on sediment and terrestrial toxicity are nonetheless considered to be representative for all PFA category members since· the category members only differ by the length of the alkyl chain* […] *and· the data on the toxicity to aquatic organisms show little evidence of differences in the toxicity with changing chain length* […]".

13 You provide the following additional reasoning for the prediction of fate properties:

- "*all PFA category members are surface-active substances according to the criteria in EU test method A.5 (Council Regulation (EC) No 440/2008)"*;
- Consistent data are available for most category member showing ready biodegradability based on reliable studies. This interpretation is supported by mechanistic considerations;
- The biodegradation pathway of alkyl amines demonstrates that they are completely mineralised by microorganisms;
- "*The alkyl chain length has little or no effect on biodegradation of primary amines by pure cultures*" and "*the degradation rates are expected to be similar due to mechanistic considerations*".

14 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance based on an identified trend within the group.

15 We have identified the following issues with the predictions of (eco)toxicological and fate properties:

0.1.2.1. Characterisation of the substances tested

16 Annex XI, Section 1.5 of the REACH Regulation provides that "substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as a group."

17 According to the Guidance on IRs and CSA, Section R.6, "in identifying a category, it is important that all potential category members are described as comprehensively as possible", because the purity profile and composition can influence the overall toxicity/properties of the potential category members (Guidance on IRs and CSA, Section R.6.2.4.1.). Therefore, qualitative and quantitative information on the compositions of the category members must be provided to confirm the category membership.

18 Furthermore, the provided information for categories consisting of UVCB (Unknown or Variable composition, Complex reaction products or of Biological materials) substances needs to include qualitative compositional information of the individual constituents of the category members; as well as quantitative characterisation in the form of information on the concentration of the individual constituents of these substances; to the extent that this is measurable (Guidance on IRs and CSA, Section R.6.2.5.5.).

19 In your read-across justification document, you state that "[a]*ll PFA category members are manufactured by catalytic hydrogenation of nitriles obtained from fatty acids. Due to the similarity of the reactions, only minor differences in the impurity profiles may be expected, which however will not affect the overall toxicity of the substances under consideration*". You also report the typical chain length distribution of the category members.

20 In your read-across justification document, you have provided compositional information for the source substances dodecan-1-amine (EC No. 204-690-6) and octadecan-1-amine (EC No. 204-695-3). For the other substances, you provide a table showing previously used names/identifiers and/or commercial names. In particular, you state that amines, coco alkyl "*was used for both C12-14- and C12-18C18u PFA category members and was split in two REACH substances in order to comply with the REACH substance identification principles*". For octadec-9-en-1-amine also referred to as oleylamine, you state that these "*descriptors relate to commercial/technical grade material*". You have provided no further information on the composition of the source substances including purity, typical C-chain length distribution and presence of unsaturation.

21 In the absence of qualitative and quantitative information on the compositions of the selected source substances, the category membership of these substances cannot be confirmed. Furthermore, simnilarity of these source substances with the category members cannot be assessed.

0.1.2.2. Data density

22 Annex XI, Section 1.5. provides that "substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances".

23 According to the Guidance on IRs and CSA, Section R.6.2.1.5., one of the factors in determining the robustness of a category is the density and distribution of the available data across the category. To identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the category members needs to be available.

- For in vitro genotoxicity (in vitro cytogenicity study in mammalian cells, and in vitro gene mutation study in mammalian cells), and reproductive and developmental toxicity (screening study, and pre-natal developmental toxicity study)

24 You have provided information on a single source substance (either amines, tallow alkyl with EC No. 263-125-1 or octadec-9-en-1-amine with EC No. 204-015-5).

- For long-term toxicity on terrestrial invertebrates and long-term toxicity on terrestrial plants

25 You have provided information on a single source substance (either amines, tallow alkyl with EC No. 263-125-1 or amines, hydrogenated tallow alkyl with EC No. 262-976-6). As explained above, you argue that this information is sufficient to cover all PFA category members since "*the category members only differ by the length of the alkyl chain* […] *and the data on the toxicity to aquatic organisms show little evidence of differences in the toxicity with changing chain length* […]".

26 Information for a single source substance is not sufficient to establish a trend across the category consisting of 7 substances. Furthermore, as explained above, you have not provided adequate information on the selected source substance to compare its composition to those of the category members. Finally, as explained under requests 2, 3, 8, 11 and 12, the information on aquatic toxicity from your dossier is not reliable and hence cannot be used to demonstrate similar aquatic toxicity properties.

27 Therefore, the information provided is not sufficient to conclude that toxicological and ecotoxicological properties are likely to follow a regular pattern.

0.1.2.3. Adequacy and reliability of source studies

28 According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

(1) be adequate for the purpose of classification and labelling and/or risk assessment;

(2) have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);

(3) cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

29 Specific reasons why the studies on the source substances do not meet these criteria are explained further under the applicable information requirement in sections 1 to 10, and 15 to 18. Therefore, no reliable predictions can be made for these information requirements.

0.1.3. Conclusion on the read-across approach

30 For the reasons above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approach under Annex XI, Section 1.5. is rejected.

31 In the comments to the draft decision, you note that "*that the grouping approach used for the REACH registration of PFAs is identical to the grouping approach used by the German competent authority in the former EU risk assessment programme on existing substances governed by Council Regulation (EC) 793/93 to evaluate the same primary fatty amines* […] *and which also served as the basis for a CLH report regarding a harmonized classification and labelling of the five different primary fatty amines under discussion*".

32 You acknowledge that "*some improvements are possible concerning the quality and availability of data to further justify the chosen evaluation approach and that additional analytical as well as toxicity data will increase the robustness of the introduced adaptations*" but you consider that "*the validity of the used 'many-to-many' read-across approach in our opinion remains unaffected*".

33 ECHA acknowledges the relevant evaluations carried out by other EU bodies or Member States. Under compliance check ECHA examines the compliance of the submitted read-across adaptations against the requirements of Annex XI, Section 1.5. In this context, section 0.1.2 above states the reasons for the rejection of the proposed adaptation which rely solely on quality issues with the supporting documentation (lack of clear characterisation of the source substances; Section 0.1.2.1), quality issues with the provided studies (Section 0.1.2.3) and low data density for some endpoints (Section 0.1.2.2). ECHA did not identify issues in relation to the scope of the grouping (Section 0.1.1.). ECHA acknowledges your intention to improve your adaptations through further data generation. However, as this strategy relies essentially on data which is yet to be generated, no conclusion on compliance can currently be made.

0.2. Weight of evidence

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

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Sub-chronic toxicity study (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2., Column 2)

35 Your weight of evidence adaptation raises the same decifiency irrespective of the information requirement for which it is invoked. Accordingly, ECHA addressed these deficiencies in the present Appendix, before assessing the specific standard information requirements in the following appendices.

36 Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

37 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study.

38 Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach.

39 However, for each relevant information requirement, you have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/assumption that the Substance has or has not a particular dangerous property.

40 In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation.

0.2.1. Issues for all endpoints

41 All endpoints adapted by applying weight of evidence rely on sources of information on an analogue substance.

42 However, as explained in section 0.1, your read-across approach under Annex XI, Section 1.5. is rejected.

0.2.2. Endpoint-specific issues

43 Your weight of evidence approach has deficiencies that are specific for these information requirements individually. The specific deficiencies are set out under the information requirement concerned in the Appendices below.

Reasons related to the information under Annex VII of REACH

1. In vitro gene mutation study in bacteria

44 An in vitro gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

1.1. Information provided

45 You have adapted this information requirement by using weight of evidence based on the following experimental data:

(i) *In vitro* gene mutation study in bacteria (1988) with amines, coco alkyl, EC No. 262-977-1.
(ii) *In vitro* gene mutation study in bacteria (1988) with the category member amines, tallow alkyl, EC No. 263-125-1.
(iii) *In vitro* gene mutation study in bacteria (1988) with the category member octadecan-1-amine, EC No. 204-695-3.
(iv) *In vitro* gene mutation study in bacteria (1985) with octadec-9-en-1-amine, EC No. 204-015-5.

1.2. Assessment of the information provided

1.2.1. Weight of evidence adaptation is rejected

46 Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

47 According to ECHA Guidance R.4.4, a weight of evidence adaptation involves an assessment of the relative values/weights of different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance of the information for the given regulatory information requirement. Subsequently, relevance, reliability, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

48 As explained in the Appendix on Reasons common to several requests, it would be sufficient to reject your weight-of-evidence adaptation based on the fact that you have not submitted any justification of your adaptation.

49 Nevertheless, ECHA has further assessed the information submitted in support of your weight of evidence adaptation and identified the following issue:

50 To fulfil the information requirement, normally a study performed according to OECD TG 471 must be provided. OECD TG 471 requires the study to investigate the following key parameter:

- detection and quantification of gene mutation (base pairs, substitution or frame shift) in cultured bacteria including data on the number of revertant colonies.

51 The sources of information i., ii., iii., and iv. investigate the above mentioned key parameter.

52 However, the reliability of the sources of information i., ii., iii., and iv. is significantly affected by the following deficiency:

53 To fulfil the information requirement, the study must meet the requirements of OECD TG 471 (2020). Therefore, the following specifications must be met:

a) The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).
b) Triplicate plating must be used at each dose level.
c) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
d) The number of revertant colonies per plate for the concurrent negative control must be inside the historical control range of the laboratory.
e) The mean number of revertant colonies per plate must be reported for the treated doses and the controls.

54 The studies i., ii., iii., and iv. are described as in vitro gene mutation study in bacteria. However, the following specifications are not according to the requirements of OECD TG 471 (2020):

a) The reported data for the study iv. you have provided did not include results for the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).
b) The reported data for the studies i., ii., iii. you have provided did not include triplicate plating at each dose level.
c) The reported data for the studies i., ii., iii., iv. you have provided did not include a positive control that produced a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
d) The reported data for the studies i., ii., iii., iv. you have provided did not include a negative control with a number of revertant colonies per plate inside the historical control range of the laboratory.
e) The reported data for the studies i., ii., iii., iv. you have provided did not include data on the number of revertant colonies per plate for the treated doses and the controls.

55 The information provided does not cover several of the key parameters required by OECD TG 471.

56 Therefore the sources of information i., ii., iii., and iv. are vitiated by the significant deficiencies identified above that affect their contribution to the conclusion on the key parameter investigated by the required study.

57 As a conclusion, the sources of information as indicated above, provide information on in vitro gene mutation study in bacteria. However, the reliability of these sources of information is affected by significant deficiencies.

58 Accordingly, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 471 study. Therefore, your adaptation is rejected and the information requirements is not fulfilled.

1.3. Specification of the study design

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

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

2. Short-term toxicity testing on aquatic invertebrates

61 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

2.1. Information provided

62 You have provided:

(i) a study according to OECD TG 202 with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 2006
(ii) a study according to TG 202 with octadec-9-en-1-amine with CAS RN 112-90-3 (EC No. 204-015-5), 2006
(iii) a study according to OECD TG 202 with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 1994
(iv) a study according to OECD TG 202 with the category member octadecan-1-amine with CAS RN 124-30-1 (EC No. 204-695-3), 1994
(v) a study according to OECD TG 202 with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 1991
(vi) a study according to OECD TG 202 with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 1986
(vii) a study according to OECD TG 202 with Amines, hydrogenated tallow alkyl with CAS RN 61788-45-2 (EC No. 262-976-6), 1995
(viii) a study according to TG 202 with octadec-9-en-1-amine with CAS RN 112-90-3 (EC No. 204-015-5), 1995
(ix) a study according to OECD TG 202 with the Substance, 2010

2.2. Assessment of the information provided

2.2.1. The proposed category approach is rejected

63 For the reasons explained under the section on Reasons common to several requests, your category approach for studies (i) to (viii) is rejected.

2.2.2. The provided studies on the Substance or the category members do not meet the information requirement

64 To fulfil the information requirement, a study must comply with OECD TG 202 and the requirements of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

65 Key parameter to be measured

a) the concentration of the test material leading to the immobilisation of 50% of daphnids at the end of the test is estimated.

66 Characterisation of exposure

b) analytical monitoring of exposure concentrations must be conducted.
c) the concentrations of the test material are measured at least at the beginning and end of the test. For volatile, unstable, or strongly adsorbing test substances, additional samplings for analysis at 24-hour intervals is required.
d) the effect values can only be based on nominal or measured initial concentration if the concentration of the test material has been satisfactorily maintained within 20 % of the nominal or measured initial concentration throughout the test (see also Guidance on IRs and CSA, Section R.7.8.4.1).

67 Additional requirements applicable to difficult to test substances

e) for adsorbing test chemical, dissolved total organic carbon concentrations (other than that due to the test chemical) must be maintained in all test solutions at or below 2 mg/L.

68 Reporting of the methodology and results

f) information on the test material is provided, including purity, chemical identity of impurities and identity and quantitative occurrence of the constituents.
g) the test design is reported (*e.g.,* static or semi-static test, number of replicates).
h) the test procedure is reported (*e.g.,* composition of the test medium, loading in number of *Daphnia* per test vessel).
i) the results of the analytical determination of exposure concentrations are provided.

69 Your registration dossier provides OECD TG 202 studies showing the following:

70 Key parameter measured

a) for study vii. above, the concentration of the test material leading to the immobilisation of 50% of daphnids at the end of the test was not estimated as it was found to be below the lowest test concentration of 1 mg/L.

71 Characterisation of exposure

b) for study iii. to vi. above, no analytical monitoring of exposure concentration was conducted.
c) the substance is considered to be highly adsorptive as it is surface active, ionised under environmentally relevant pH and it has a reported log Kow of 4.33. For studies i., ii. and viii., you have observed significant loss from the test medium at t=48h. However, additional samplings for analysis at 24-hour intervals were not conducted.
d) for studies i., ii. and viii., you expressed the effect values based on nominal concentrations while > 20% loss of the substance was observed by the end of the test.

72 Additional requirements applicable to difficult to test substances

e) as explained above, the substance is considered to be highly adsorptive. For studies i. and ii. above, you report that the test was conducted with natural freshwater with a TOC content of 7.1 mg/L. For study viii. above, the test was conducted without humic acid or with addition of 10 or 20 mg/L humic acid. In this study, the test medium used was Dutch Standard water with a TOC content of 2.269 mg/L. For study ix., your report that the test was conducted with natural river water with a TOC content of 5.89 mg/L.

73 Reporting of the methodology and results

f) for studies i., iii., v. and viii. above, you have provided information on the purity of the test material. However, you have provided no information on impurities or identity and quantitative occurrence of the constituents (in particular their C-chain length distribution). For studies iv., vi. and vii. above, you have only provided the identifiers of the test material but no qualitative or quantitative information on its composition.
g) for study vi. above, you have provided no information on the test design.
h) for study vi. above, you have provided no information on the test procedure. Furthermore, for studies iii. and iv., you specify that the test medium was "freshwater". However, you provide no information on the composition of the medium, including TOC content.
i) for study vii., the results of the analytical determination of exposure concentrations are not provided.

74 Based on the above,

- the key parameter of OECD TG 202 is not covered in study vii.
- there are critical methodological deficiencies resulting in the rejection of the results of these studies. More, specifically
  - exposure has not been verified analytically for studies iii. to vi.;
  - for studies i., ii., and viii., sampling was no conducted with an appropriate frequency;
  - for studies i., ii., viii. and ix. above, the TOC content of the test medium was above the mandatory value of 2 mg/L. On the latter, ECHA notes that individual opinions of ECHA's Risk Assessment Committee (RAC) are available on some Primary Alkyl Amines (i.e. EC No. 204-015-5, EC No. 204-695-3, EC No. 262-977-1, EC No. 263-125-1, EC No. 262-976-6) where RAC concluded that, for studies conducted with a dilution water containing a high level of suspended matter and humic acid, nominal concentrations do not represent truly dissolved concentrations and that therefore such studies have limited usefulness for the purposes of classification. In this context, ECHA further notes that the Guidance on Application of CLP Criteria (Section 1.1.3.) clarifies that classification must be based on intrinsic hazards, i.e. the basic properties of a substance as determined in standard tests or by other means designed to identify hazards. As the CLP Regulation is hazard-based, the data on intrinsic properties must not take exposure into consideration. Therefore, the bulk approach which aims at mimicking exposure under "more environmentally realistic" conditions must not be used for classification and labelling. As already explained above, this conclusion was confirmed by RAC, among other cases, for primary alkyl amines. Similar considerations apply for the PBT assessment. As per Annex XIII of REACH, the PBT assessment should be based on data generated under 'relevant conditions', i.e. those conditions that allow for an objective assessment of the PBT/vPvB properties of a substance and not the PBT/vPvB properties of a substance in particular environmental conditions. This has been also confirmed by the Board of Appeal in its Decision of 7 December 2016 in case A-013-2014.
- the reporting of studies i. and iii. to viii. is not sufficient to conduct an independent assessment of their reliability. More specifically,
  - you have not provided adequate information on the test material in any of these studies;
  - for study vi. above, you have not provided adequate information on the study design and procedure and therefore it is unclear if this study meets the specification of OECD TG 202
  - for studies iii. and iv. above, you have not provided adequate information to verify whether TOC content in the test medium was below the mandatory value of 2 mg TOC/L.

75 Therefore, the requirements of OECD TG 202, in conjunction with OECD GD 23, are not met for any of the reported studies.

76 For all the reasons explained above, the information requirement is not fulfilled.

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

2.3. Study design and test specifications

78 The Substance is difficult to test due to its surface active (surface tension reported as equal to 28.15 mN/m in Section 4.10 of your dossier) and adsorptive properties (Log Kow reported as equal to 4.33 in Section 4.7 of your dossier). OECD TG 202 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or

other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e., measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

3. Growth inhibition study aquatic plants

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

3.1. Information provided

80 You have provided:

(i) a study according to OECD TG 201 with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 2002
(ii) a study according to OECD TG 201 with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 2002
(iii) a study according to OECD TG 201 with octadec-9-en-1-amine with CAS RN 112-90-3 (EC No. 204-015-5), 2002
(iv) a study according to OECD TG 201 with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 1991
(v) a study according to OECD TG 201 with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 1991
(vi) a study according to OECD TG 201 with Amines, hydrogenated tallow alkyl with CAS RN 61788-45-2 (EC No. 262-976-6), 1991
(vii) a study according to OECD TG 201 with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 1994
(viii) a study according to OECD TG 201 with Amines, hydrogenated tallow alkyl with CAS RN 61788-45-2 (EC No. 262-976-6), 1994
(ix) a study according to OECD TG 201 with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 1996
(x) a study according to OECD TG 201 with octadec-9-en-1-amine with CAS RN 112-90-3 (EC No. 204-015-5), 1995
(xi) a study according to OECD TG 201 on the Substance, 2010

3.2. Assessment of the information provided

3.2.1. The proposed category approach is rejected

81 For the reasons explained under the section on Reasons common to several requests, your category approachfor the studies (i) to (x) is rejected.

3.2.2. The provided studies on the Substance or the category members do not meet the information requirement

82 To fulfil the information requirement, a study must comply with OECD TG 201 and the requirements of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

83 Characterisation of exposure

a) analytical monitoring must be conducted.
b) the concentrations of the test material are measured at least at the beginning and end of the test:
    i. at the highest, and
    ii. at the lowest test concentration, and
    iii. at a concentration around the expected EC_{50}.
c) the concentrations of the test material are measured at least at the beginning and end of the test. For volatile, unstable or strongly adsorbing test substances, additional samplings for analysis at 24-hour intervals is required.
d) the effect values can only be based on nominal or measured initial concentration if the concentration of the test material has been satisfactorily maintained within 20 % of the nominal or measured initial concentration throughout the test (see also Guidance on IRs and CSA, Section R.7.8.4.1).

84 Additional requirements applicable to difficult to test substances

e) for adsorbing test chemical, dissolved total organic carbon concentrations (other than that due to the test chemical) must be maintained in all test solutions at or below 2 mg/L.

85 Reporting of the methodology and results

f) information on the test material is provided, including purity, chemical identity of impurities and identity and quantitative occurrence of the constituents.
g) the test conditions are reported (*e.g.*, composition of the test medium, including TOC content).
h) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

86 Your registration dossier provides OECD TG 201 studies showing the following:

87 Characterisation of exposure

a) for studies iv. to ix. above, no analytical monitoring of exposure concentration was conducted.
b) for studies i. to iii., analytical monitoring was only conducted on the highest test concentration.
c) As explained under Appendix 1.2., the substance is considered ot be highly adsorptive. For studies i. to iii. and xi., you have observed significant loss from the test medium at t=72h. However, additional samplings for analysis at 24-hour intervals were not conducted. The same applies to study x.
d) for studies i. to iii., x. and xi., you expressed the effect values based on nominal concentrations while > 20% loss of the substance was observed by the end of the test.

88 Additional requirements applicable to difficult to test substances

j) as already explained under Appendix 1.2., the substance is considered to be highly adsorptive. For studies i. to iii., you report that the test was conducted with natural freshwater with a TOC content of 9.9 mg/L. For study x. above, the test was conducted without humic acid or with addition of 5 or 10 mg/L humic acid. In this study, the test medium without addition of humic acid had a TOC content of 4.45 mg/L. For study xi., your report that the test was conducted with natural river water with a TOC content of 5.89 mg/L.

89 Reporting of the methodology and results

e) for studies i. to vi. and x. above, you have provided information on the purity of

the test material. However, you have provided no information on impurities or identity and quantitative occurrence of the constituents (in particular their C-chain length distribution). For studies vii. to ix. above, you have only provided the identifiers of the test material but no qualitative or quantitative information on its composition.

f) on the test conditions, you have not specified the composition of the test medium, including the TOC content for studies iv. to ix.

g) tabulated data on the algal biomass determined daily for each treatment group and control are not reported for studies i. to x.

90 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the results of these studies. More, specifically
  - exposure has not been verified analytically for studies iv. to ix;
  - for studies i. to iii., x. and xi., sampling was no conducted with an appropriate frequency (and on all required test concentration for studies i. to iii.);
  - for studies i. to iii. and x. to xi., the TOC content of the test medium was above the mandatory value of 2 mg/L. As already explained under Appendix 1.2., testing with high TOC test medium does not provide relevant data for the purpose of classification and labelling and PBT assessment and is therefore not acceptable.
- the reporting of studies i. to x. is not sufficient to conduct an independent assessment of their reliability. More specifically,
  - you have not provided adequate information on the test material in any of these studies;
  - for studies iv. to ix., you have not provided adequate information to verify whether TOC content in the test medium was below the mandatory value of 2 mg TOC/L;
  - for studies i. to x., you have not provided measured biomass data. Therefore, it is not possible to verify whether the validity criteria of the OECD TG 201 were met and to verify the interpretation of the results of these studies.

91 Therefore, the requirements of OECD TG 201, in conjunction with OECD GD 23, are not met for any of the reported studies.

92 For all the reasons explained above, the information requirement is not fulfilled.

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

3.3. Study design and test specifications

94 OECD TG 201 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix 1.2.

95 In your comments to the draft decision, you explain that the substance is difficult to test and that available studies indicate that "plausible results are only possible by performing them in a semi-static or flow-through design, which is not possible in a study with algae". You query whether "*the endpoint toxicity to aquatic plants can reliable be fulfilled with data generated in astatic test with organism that have such a high surface area, like the preferred species algae*". You propose to "*conduct range-finding studies with at least two substances* [from the category] *to develop a suitable system and to clarify that algae and Lemna are of comparable sensitivity*" and "*if the results of the range-finders show*

comparable findings combined with better analytical recoveries full Lemna studies will be considered instead of algae studies".

96 ECHA acknowledges that it may be difficult to maintain 'close-to-nominal' dissolved concentrations of the test substance in a study conducted according to OECD TG 201. In this context, paragraph 40 of the OECD TG 201 specifies that "*the actual exposure concentrations may be difficult to define, especially for adsorbing substances tested at low concentrations. In such cases, disappearance of the test substance from solution by adsorption to the increasing algal biomass does not mean that it is lost from the test system. When the result of the test is analysed, it should be checked whether a decrease in concentration of the test substance in the course of the test is accompanied by a decrease in growth inhibition. If this is the case, application of a suitable model describing the decline of the concentration of the test substance (7) may be considered*".

97 ECHA further acknowledges that the OECD TG 221 may be used to meet this information requirement. However, as explained in Appendix R.7.8—2, such study on vascular plants are only regarded as informing on acute toxicity.

4. Ready biodegradability

98 Ready biodegradability is an information requirement in Annex VII to REACH (Section 9.2.1.1.).

4.1. Information provided

99 You have provided:

(i) a study according to OECD TG 301B with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 1996
(ii) a study according to OECD TG 301B with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 1996
(iii) a study according to OECD TG 301B with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 1992
(iv) a study according to OECD TG 301B with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 1992
(v) a study according to OECD TG 301B with Amines, hydrogenated tallow alkyl with CAS RN 61788-45-2 (EC No. 262-976-6), 1992
(vi) a study according to OECD TG 301D with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 1992
(vii) a study according to OECD TG 301D with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 1992
(viii) a study according to OECD TG 301D with Amines, hydrogenated tallow alkyl with CAS RN 61788-45-2 (EC No. 262-976-6), 1992
(ix) a study according to OECD TG 301D with octadec-9-en-1-amine with CAS RN 112-90-3 (EC No. 204-015-5), 1992
(x) a study according to OECD TG 301F with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 1994
(xi) a study according to OECD TG 301F with the category member octadecane-1-amine with CAS RN 124-30-1 (EC No 204-695-3), 1994
(xii) a study according to OECD TG 301B with octadec-9-en-1-amine with CAS RN 112-90-3 (EC No. 204-015-5), 1994
(xiii) a study according to OECD TG 301D with the Substance, 1994 (report number: 94-0165-43)
(xiv) a reference to a scientific report on the degradation of the category member Amines, tallow alkyl, 1998

(xv) a study according to OECD TG 301D with the Substance, 1994 (report number: CRL F94011)

4.2. Assessment of information provided

4.2.1. The proposed category approach is rejected

100 For the reasons explained under the section on Reasons common to several requests, your category approach for the studies (i) to (xiii) and (xiv) is rejected.

4.2.2. The provided studies on the Substance or the category members do not meet the information requirement

101 To fulfil the information requirement, a study must comply with the OECD TG 301 or 310 (Article 13(3) of REACH). Therefore, for a study according to OECD TG 301, the following requirements must be met:

102 Validity criteria

a) for a study according to OECD TG 301B, the total CO_2 evolution in the inoculum blank at the end of the test does not normally exceed 40 mg CO_2/L.

103 Technical specifications impacting the sensitivity/reliability of the test

b) the inoculum is not pre-adapted to the test material.
c) for a study according to OECD TG 301D, test solutions are prepared using an appropriate nutrient medium, which includes ammonium chloride.
d) when solvents or emulsifying agents are used to increase the homogeneity of test solutions when testing poorly soluble substances, a blank run containing the auxiliary substance is included in the test design which must demonstrate that the solvent or emulsifier:
    - is not toxic to bacteria, and/or
    - is not biodegraded, and/or
    - does not cause foaming under the test conditions.

104 Reporting of the methodology and results

e) information on the test material is provided, including purity, chemical identity of impurities and identity and quantitative occurrence of the constituents.
f) the test conditions are reported (e.g., adaptation of inoculum (if any), density of the inoculum in cells/mL and in mg/L suspended solid, test medium composition
g) for a study according to OECD TG 301B, the inorganic carbon content (IC) and total carbon content (TC) of the test material suspension in the mineral medium at the beginning of the test is reported.
h) for a study according to OECD TG 301B, the calculation of the $ThCO_2$ is described and justified.
i) for a study according to OECD TG 301D and 301F, the calculation of the ThOD is described and justified.
j) for a study according to OECD TG 301D or 301F on nitrogen-containing test materials, correction for nitrification is applied on the theoretical oxygen demand (*i.e.* $ThOD_{NO3}$) unless it can be demonstrated that nitrification did not occur (*e.g.* by monitoring changes in concentrations in nitrite and nitrate).
k) the results of measurements at each sampling point in each replicate is reported in a tabular form.

105 Your registration dossier provides OECD TG 301 studies showing the following:

106 Validity criteria

a) for studies i. to ii., the total CO_2 evolution in the inoculum blank at the end of the test was 74.4 mg CO_2/L.

107 Technical specifications impacting the sensitivity/reliability of the test

b) for study x., you specified that the inoculum was adapted to the test material.
c) for studies vi. to ix., you report that "*Ammonium chloride was omitted from the medium to prevent nitrification*".
d) for study xii., you report that Dichloro-1,1 fluoro-1 ethane was used as a solubilising agent. However, you have not provided the results of a blank run using the containing the auxiliary substance.

108 Reporting of the methodology and results

e) for studies iii. to v., you report the test material as corresponding to "*100% technical Grade Product*". For studies vi. to x. and xii. you provide information on purity. However, you have provided no information on impurities or identity and quantitative occurrence of the constituents (in particular their C-chain length distribution) for any of these studies. For studies i. and ii., xi. and xv. above, you have only provided the identifiers of the test material but no qualitative or quantitative information on its composition. For study xiv., you refer to the test material as "Amines, tallow alkyl" without any identifiers or compositional information.
f) Concerning the adaptation of the inoculum, for studies iii. to viii., xi. to xii. and xiv., you have not specified whether the inoculum was adapted to the test material prior to the test. Concerning the inoculum density, for studies iii. to v. (Closed bottle test), you report that a filtrate of a sewage sludge was used as inoculum and you report that the filtrate was used at a rate of 1% of the final volume of the test solution. For studies vi. to ix. and xiv., you state that "*The sludge was diluted to a concentration in the BOD bottles of 2 mg DW/L*". For study xi., you report inoculum density as "*13.5 ml/L (wet sludge); 30 mg/L (dry weight)*". However, you have provided no information on inoculum density as cells/L for these studies. For study x., xiii. And xv., you have provided no information on inoculum density. Concerning the composition of the test medium, you have provided no information on test medium composition for studies iii. to v., xiii and xv.
g) the inorganic carbon content (IC) and total carbon content (TC) of the test material suspension in the mineral medium at the beginning of the test is not reported in studies i. to v. and xiii.
h) for a studies i. to v., the calculation of the $ThCO_2$ is not described.
i) for a studies vi. to xii. And xv., the calculation of the ThOD is not described.
j) for studies vi. to x. and xiii. to xv., you have not specified if the results were corrected for nitrification (or alternatively supporting information that nitrification did not occur).
k) for a studies iii. to v. and xii. to xv., the results of measurements at each sampling point in each replicate is not provided.

109 Based on the above,

- the validity criteria of OECD are not met in studies i. and ii. For studies i. and ii., the total CO2 evolution in the inoculum blank at the end of the test was above the maximum tolerable value. ECHA notes that the OECD TG 301B states that "*if values greater than 70 mg CO2/l are obtained, the data and experimental technique should be examined critically*". However, you have provided no justification as to why this deviation did not impact the reliability of these studies.
- there are critical methodological deficiencies resulting in the rejection of study vi. to x. and xii. More, specifically:
  - study x. was conducted with an adapted inoculum and cannot therefore be

used to conclude on ready biodegradability.
    - studies vi. to ix. were conducted with a test medium containing no ammonium chloride. This may have artificially reduced respiration in the inoculum blank (i.e., one of the validity criteria of OECD TG 301D).
    - study xii. Was conducted with an auxiliary solvent. However, you have provided no justification that the solvent is not biodegraded during the test and that it did not bias the study results.
- the reporting of all studies is not sufficient to conduct an independent assessment of its reliability. More, specifically:
    - you have not provided adequate information on the test material in any of these studies.
    - the reporting of study xiv. does not provide an unambiguous description on how the study(ies) was(were) conducted. Further, the reporting lacks essential elements on the study design, study methodology and results as listed above under 'Reporting of the methodology and results'.
    - you have not described and justified how the ThCO2 (for studies according to OEDC TG 301B) or ThOD (for studies conducted according to OECD TG 301D or 301F) was calculated. Furthermore, for studies vi. to x., xiii. and xv., you have not specified if the results were corrected for nitrification. ECHA notes that for most of the reported studies, the results are below or slightly higher to the cut-off value to conclude on ready biodegradability. In this absence of this information, ECHA cannot assess whether the interpretation of the results are correct.
    - a number of key information are missing for most studies. The IC and TC of of the test material suspension in the mineral medium at the beginning of the test is not reported in studies i. to v. and xii. which is needed to assess the validity criteria of OECD TG 301B. For studies iii. to ix. and xi. to xii., you have not specified whether the inoculum was adapted to the test meterial prior to the test and therefore if these studies qualify for a ready biodegradability study. The inoculum density is also unclear in studies iii. to xi., xiii. and xv. and, therefore, it cannot be verified whether the studies were conducted under acceptable test conditions. Also, you have not specified the test medium composition in studies iii. to v., xiii and xv.
    - for a studies iii. to v. and xii. to xiii. and xv., the results of measurements at each sampling point in each replicate is not provided. Therefore, irrespective of the issues listed above, an independent assessment of the results of these studies and their interpretation is not possible.

110 Therefore, the requirements of OECD TG 301 are not met for any of the reported studies.

111 In your comments to the draft decision, you explain that all missing parameters listed aboved for studies i., ii. and vi. to ix. will be included in your dossier following a dossier update.

112 This information has not been provided as part of your comments to the draft decision and is not present in the IUCLID dossier. Therefore, no conclusion on the adequacy can currently be made.

113 Finally, you also consider the omission of ammonium chloride from the test medium used in studies vi. to ix as a minor deviation. You claim that this conclusion was supported in a previous compliance check decision (e.g. CCH-D-2114522376-51-01/F, page 14).

114 ECHA considers that there were case specific considerations which explain why this deviation was considered of secondary importance in the earlier compliance check decision that you are referring to. In particular, the respiration in the inoculum blank after 28 days was well below the cut-off value value of 1.5 mg O2/L in the corresponding studies (*i.e.*,

0.5 mg O2/L) and it can be reasonably assumed that it would have still remained under that value in the presence of ammonium chloride. However, in the studies vi. to ix., the respiration in the inoculum blank after 28 days was already *c.a.* two times higher (i.e. 0.9 mg/L) in the absence of ammonium chloride. The concentration of oxygen in the mineral nutrient solution with inoculum was in average 9.0 mg/L and 8.1 mg/L at day 0 and day 28, respectively. This corresponds to an oxygen depletion of 0.9 mg dissolved oxygen/L after 28 days. Therefore, higher uncertainty exists as to whether it would have remained below 1.5 mg/L if a standard test medium had been used.

115 For all the reasons explained above, the information requirement is not fulfilled.

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

Reasons related to the information under Annex VIII of REACH

5. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

117 An in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

5.1. Information provided

118 You have adapted this information requirement by using weight of evidence based on the following experimental data:

(i) *in vitro* mammalian chromosome aberration test (1985) with Oleyl Alkylamines, EC No. 204-015-5.

5.2. Assessment of the information provided

5.2.1. Weight of evidence adaptation is rejected

119 In addition to the issues raised in the Appendix on Reasons common to several requests, ECHA has further assessed the information submitted in support of your weight of evidence adaptation and identified the following issues:

5.2.1.1. Weight of evidence cannot rely on one source of information

120 Irrespective of this deficiency, which in itself leads to the rejection of the adaptation, ECHA has assessed the provided source of information and also found the following deficiency.

5.2.1.2. The provided study does not meet the information requirement

121 To fulfil the information requirement the study has to be an in vitro chromosomal aberration test or an in vitro micronucleus test, conducted in mammalian cells in accordance with OECD TG 473 or OECD TG 487, respectively (Guidance on IRs and CSA, Table R.7.7–2). Therefore, the following specifications must be:

a) The maximum concentration tested must induce 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration must correspond to 10 mM, 2 mg/mL or 2 µl/mL, whichever is the lowest.
b) At least 300 well-spread metaphases must be scored per concentration.
c) The response for the concurrent negative control must be inside the historical control range of the laboratory.
d) Data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures must be reported.

122 The study i. is described as in vitro mammalian chromosome aberration test. However, the following specifications are not according to the requirements of OECD TG 473:

a) a maximum tested concentration of 10 mM, 2 mg/mL or 2 µl/mL, or that induced 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance.
b) the scoring of at least 300 metaphases per concentration.
c) a negative control with a response inside the historical control range of the laboratory.
d) data on the cytotoxicity and/or the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures.

123 The information provided does not cover key parameters required by OECD TG 473.

124 Therefore, your adaptation is rejected and the information requirements is not fulfilled.

5.3. Specification of the study design

125 To fulfil the information requirement for the Substance, either in vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or in vitro micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

126 In the comments to the draft decision you present a strategy relying on the generation of additional supporting information (from a bacterial reverse mutation assay and the extended ToxTracker Aneugen Clastogen Evaluation (ACE) assay) on each of the category members. You indicate your intention to perform an *in vitro* genotoxicity study on selected category members thereafter.

127 ECHA acknowledges your intentions to improve the genotoxicity profile of the category members and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

6. In vitro gene mutation study in mammalian cells

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

6.1. Triggering of the information requirement

129 Your dossier contains data for an in vitro gene mutation study in bacteria, and data for an in vitro cytogenicity study in mammalian cells or in vitro micronucleus study.

130 The information for the in vitro gene mutation study in bacteria and for the in vitro cytogenicity study in mammalian cells provided in the dossier are rejected for the reasons provided in sections 1 and 5.

131 The result of the requests for an in vitro gene mutation study in bacteria and for an in vitro cytogenicity study in mammalian cells will determine whether the present requirement for an in vitro mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

132 Consequently, you are required to provide information for this endpoint, if the in vitro gene mutation study in bacteria and the in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study provide a negative result.

6.2. Information provided

133 You have adapted this information requirement by using weight of evidence based on the following experimental data:

(i) *In vitro* mammalian cell gene mutation test (1985) with octadec-9-en-1-amine, EC No. 204-015-5.
(ii) *In vitro* mammalian cell gene mutation test (1989) with octadec-9-en-1-amine, EC No. 204-015-5.

6.3. Assessment of the information provided

6.3.1. Weight of evidence adaptation is rejected

134 In addition to the issues raised in the Appendix on Reasons common to several requests, ECHA has further assessed the information submitted in support of your weight of evidence adaptation and identified the following issue:

135 To fulfil the information requirement, normally a study performed according to OECD TG 476/490 and OECD TG 488 must be provided. OECD TG 476/490 and OECD TG 488 require the study to investigate the following key parameter:

- Detection and quantification of gene mutations (point mutations, frame-shift mutations, small deletions, etc.) including data on the frequency of mutant colonies in cultured mammalian cells (*in vitro*) or mutant frequency for each tissue in mammals (*in vivo*).

136 Only the sources of information i. and ii. provide relevant information on detection and quantification of gene mutation in cultured mammalian cells.

137 However, the reliability of these sources of information i. and ii. is significantly affected by the following deficiency:

138 To fulfil the information requirement, the study must meet the requirements of OECD TG 476/490 and OECD TG 488. Therefore, the following specifications must be met:

a) The maximum concentration tested must induce 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration must correspond to 10 mM, 2 mg/mL or 2 µl/mL, whichever is the lowest.
b) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the response compared with the concurrent negative control.
c) The response for the concurrent negative control must be inside the historical control range of the laboratory.
d) Data on the cytotoxicity and the mutation frequency for the treated and control cultures must be reported.

139 The studies i. and ii. are described as in vitro mammalian cell gene mutation studies. However, the following specifications are not according to the requirements of OECD TG 476:

a) For the study i. you have not provided a maximum tested concentration of 10 mM, 2 mg/mL or 2 µl/mL, or that induced 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance.
b) For the studies i. and ii. you have not provided one positive control that produced a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
c) For the studies i. and ii. you have not provided a negative control with a response inside the historical control range of the laboratory.
d) For the studies i. and ii. you have not provided data on the cytotoxicity and the mutation frequency for the treated and control cultures.

140 The information provided does not cover key parameters required by OECD TG 476.

141 Therefore the sources of information i. and ii. are vitiated by the significant deficiencies identified above that affect their contribution to the conclusion on the key parameter investigated by the required study.

142 As a conclusion, the sources of information i. and ii. provide information on in vitro gene mutation study in mammalian cells. However, the reliability of these sources of information is affected by significant deficiencies.

143 Accordingly, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 476/490 or OECD TG 488 study. Therefore, your adaptation is rejected and the information requirements is not fulfilled.

6.4. Specification of the study design

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

145 In the comments to the draft decision you present a strategy relying on the generation of additional supporting information (from a bacterial reverse mutation assay and the extended ToxTracker Aneugen Clastogen Evaluation (ACE) assay) on each of the category members. You indicate your intention to perform an *in vitro* genotoxicity study on selected category members thereafter.

146 ECHA acknowledges your intentions to improve the genotoxicity profile of the category members and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

7. Short-term toxicity on fish

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

7.1. Information provided

148 You have provided:

(i) a study according to OECD TG 203 with the category member dodecan-1-amine with CAS RN 124-22-1 (EC No. 204-690-6), 1988
(ii) a study according to OECD TG 203 with the category member octadecan-1-amine with CAS RN 124-30-1 (EC No. 204-695-3), 1988
(iii) a study according to OECD TG 203 with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 1988
(iv) a study according to OECD TG 201 with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 1988
(v) a study according to OECD TG 203 with octadec-9-en-1-amine with CAS RN 112-90-3 (EC No. 204-015-5), 1988
(vi) a study according to OECD TG 203 with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 1991
(vii) a study according to OECD TG 203 with Amines, hydrogenated tallow alkyl with CAS RN 61788-45-2 (EC No. 262-976-6), 1991
(viii) a study according to OECD TG 203 with octadec-9-en-1-amine with CAS RN 112-90-3 (EC No. 204-015-5), 1995
(ix) a study according to OECD TG 203 with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 2006
(x) a study according to OECD TG 203 with octadec-9-en-1-amine with CAS RN 112-90-3 (EC No. 204-015-5), 2006

(xi) a study according to OECD TG 203 with the Substance, 2010

7.2. Assessment of the information provided

7.2.1. The proposed category approach is rejected

149 For the reasons explained under the section on Reasons common to several requests, your category approach is rejected for the studies (i) to (xiii) and (xi).

7.2.2. The provided studies on the Substance or the category members do not meet the information requirement

150 To fulfil the information requirement, a study must comply with OECD TG 203 and the requirements of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

151 Validity criteria

a) the analytical measurement of test concentrations is conducted.

152 Characterisation of exposure

b) the concentrations of the test material are measured at least at the beginning and end of the test. For volatile, unstable or strongly adsorbing test substances, additional samplings for analysis at 24-hour intervals is required.
c) the effect values can only be based on nominal or measured initial concentration if the concentration of the test material has been satisfactorily maintained within 20 % of the nominal or measured initial concentration throughout the test (see also Guidance on IRs and CSA, Section R.7.8.4.1).

153 Technical specifications impacting the sensitivity/reliability of the test

d) the test is conducted on juveniles of similar age (or size).

154 Additional requirements applicable to difficult to test substances

e) for adsorbing test chemical, dissolved total organic carbon concentrations (other than that due to the test chemical) must be maintained in all test solutions at or below 2 mg/L.

155 Reporting of the methodology and results

f) information on the test material is provided, including purity, chemical identity of impurities and identity and quantitative occurrence of the constituents.
g) the test procedure is reported (*e.g.* composition of the test medium, including TOC content, mean body length of test animals);

156 Your registration dossier provides an OECD TG 203 showing the following:

157 Validity criteria

a) no analytical measurement of test concentrations was conducted for studies i. to vii.

158 Characterisation of exposure

b) as already explained under Appendix 1.2., the substance is considered to be highly adsorptive. For studies ix. to xi., you have observed significant loss from the test medium at t=48h (i.e., at the time of medium renewal in the semi-static test). Similarly, significant losses were observed in study viii. However, for these studies, you have not provided consistent measurement of exposure at 24-hour intervals.
c) for studies ix to xi., you expressed the effect values based on nominal

concentrations while > 20% loss of the substance was observed by the end of the test.

159 Technical specifications impacting the sensitivity/reliability of the test

d) studies i., iii., iv., vii., ix to xi. were conducted on *Danio rerio*. The mean body length of test animals was above the recommended length range of 1-2 cm in all these studies.

160 Additional requirements applicable to difficult to test substances

k) as already explained under Appendix 1.2., the substance is considered to be highly adsorptive. For studies ix and x. above, you report that the test was conducted with natural freshwater with a TOC content of 7.1 mg/L. For study viii. above, the test was conducted without humic acid (TOC content of c.a. 1 mg/L) or with addition of 10 or 20 mg/L humic acid, leading to a TOC content of 5.1 and 6.8 mg/L, respectively. For study xi., your report that the test was conducted with natural river water with a TOC content of 5.89 mg/L.

161 Reporting of the methodology and results

e) for studies i., iii., iv., vi. to ix. above, you provide information on purity. However, you have provided no information on impurities or identity and quantitative occurrence of the constituents (in particular their C-chain length distribution) for any of these studies. For studies ii. and v. above, you have only provided the identifiers of the test material but no qualitative or quantitative information on its composition.

f) for studies ii. and v. above, the test medium is not described. For studies i., iii. and iv., the TOC content of the test medium is not provided. For studies, ii. and v., the mean body length of test animals is not provided.

162 Based on the above,

- the key validity criteria of OECD TG 203 are not met for studies i. to vii. as no monitoring of exposure was conducted.
- there are critical methodological deficiencies resulting in the rejection of the results of these studies. More specifically,
  - sampling for analytical determination of exposure was no conducted with an appropriate frequency for studies viii. to xi. and therefore, characterisation of exposure remains uncertain;
  - studies i., iii., iv., vii. and ix to xi. were conducted on test animals that were above the range of acceptable body length for the test species. In the absence of any justification, ECHA concludes that the test was not conducted on juveniles as required by the OECD TG 203;
  - for studies viii. (with addition of humic acid), and studies ix. to xi., the TOC content of the test medium was above the mandatory value of 2 mg/L. As already explained under Appendix 1.2., testing with high TOC test medium does not provide relevant data for the purpose of classification and labelling and PBT assessment and is therefore not acceptable.
- the reporting of studies i., iii., iv., vi. to ix is not sufficient to conduct an independent assessment of their reliability. More specifically,
  - you have not provided adequate information on the test material in any of these studies;
  - in the absence of adequate information on test medium composition for studies i. to v., it is not possible to verify that TOC content was within an acceptable range;
  - in the absence of information on mean body length of test animals in studies ii. and v., it is not possible to verify whether the test was conducted on

juvenile fish.

163 Therefore, the requirements of OECD TG 203, in conjunction with OECD GD 23, are not met for any of the reported studies.

164 For all the reasons explained above, the information requirement is not fulfilled.

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

7.3. Study design and test specifications

166 OECD TG 203 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix 1.2.

Reasons related to the information under Annex IX of REACH

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

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

8.1. Information provided

168 ECHA understands that you have adapted this information requirement by using weight of evidence based on the following experimental data:

(i) Repeated Dose 28-Day Oral Toxicity Study in Rodents (2003) with octadec-9-en-1-amine, EC No. 204-015-5.

(ii) Dose-range finding study based on OECD guideline 407 for subacute 28 day study according to GLP (1999) with the category member amines, tallow alkyl, EC No. 263-125-1.

(iii) Repeated Dose 28-Day Oral Toxicity Study in Rodents (1999) with the category member amines, tallow alkyl, EC No. 263-125-1.

(iv) Publication *The chronic toxicity of octadecylamine*, [redacted] (1957) with the category member Octadecylamines, EC No. 204-695-3.

169 In addition, you refer to two publications which review the results of study iv.: The chronic toxicity of Octadecylamine, [redacted] (1958) and Final report on the safety assessment of lauramine and stearamine, [redacted] (1995).

170 Since these two publications refer to the study iv., they do not constitute an additional source of information. For this reason, these two publications were not taken into account in ECHA's assessment.

8.2. Assessment of the information provided

8.2.1. Weight of evidence adaptation is rejected

171 In addition to the issues raised in the Appendix on Reasons common to several requests, ECHA has further assessed the information submitted in support of your weight of evidence adaptation and identified the following issue:

172 To fulfil the information requirement, normally a study performed according to OECD TG 408 must be provided. OECD TG 408 requires the study to provide information on systemic toxicity in intact, non-pregnant and young adult males and females to investigate the following key parameters from:

1) in-life observations;
2) blood chemistry, and organ and tissue toxicity.

173 Information should address effects on the following physiological systems: circulatory system, digestive/excretory system, endocrine system, immune system, integumentary system, musculoskeletal system, nervous system, renal/urinary system, reproductive system, and respiratory system.

174 1) In-life observations

175 In-life observations must include information on survival, body weight development, clinical signs, functional observations, food/water consumption and other potential aspects of in life observations on the relevant physiological systems (circulatory, digestive/excretory, integumentary, musculoskeletal, nervous, renal/urinary, and respiratory).

176 The sources of information provide information on survival (i., ii., iii., and iv.), body weight development (i., ii., iii., and iv.), clinical signs (i., ii., and iii.), food consumption (i., ii., iii., and iv.) as foreseen to be investigated in OECD TG 408.

177 However, the sources of information i., ii., iii., and iv. do not provide information on water consumption and functional observations. In addition, the source of information iv. does not provide information on clinical signs on the relevant physiological systems.

178 In addition, the reliability of these sources of information is significantly affected by the following deficiencies:

179 Firstly, you have not provided robust study summaries which would allow verification of the reliability of the studies used.

180 Secondly, for the reasons explained under the section on Reasons common to several requests, your category approach is rejected.

181 Thirdly, to fulfil the information requirement, the sub-chronic toxicity study (90 day) has to meet the requirements of OECD TG 408. Therefore, the following specifications must be met:

a) highest dose level should aim to induce toxicity or reach the limit dose;
b) clinical signs observed daily and functional observations week 11 or after, i.e. sensory activity, grip strength and motor activity assessments;
c) haematological and clinical biochemistry tests as specified in paragraphs 30-38 of the test guideline;
d) the oestrus cycle in females at necropsy;
e) terminal organ and body weights;
f) gross pathology as specified in paragraphs 43-46 of the test guideline;
g) full histopathology as specified in paragraphs 47-49 of the test guideline.

182 In the sources of information i., ii. and iii., the following specifications are not according to the requirements of OECD TG 408:

- an exposure duration of 28 days (sources of information i., and iii.) or 14 days (source of information ii.)

183 In study iv., the following specifications are not according to the requirements of OECD TG 408:

a) no justification for the dose setting while the highest dose levels tested was 500 ppm (i.e., 100 mg/kg/day), which is below the limit dose of the test guideline, and no adverse effect were observed;
b) data on clinical signs and functional observations: nature, severity and duration;
c) data on haematology and clinical biochemistry findings: incidence and severity with relevant baseline values;
d) data on oestrus cycle;
e) data on terminal organ weights and organ/body weight ratios;
f) data on gross pathology findings: incidence and severity;
g) data on histopathology findings: incidence and severity.

184 Therefore, the provided studies are affected by significant deficiencies which vitiate the information on in-life observations that is normally investigated by the required study.

185 2) Blood chemistry, and organ and tissue toxicity

186 Information on blood chemistry must include haematological (full-scale) and clinical chemistry analysis (full-scale), and other potential aspects related to blood chemistry to address relevant physiological systems (circulatory digestive/excretory, endocrine, immune, musculoskeletal, and renal/urinary). Organ and tissue toxicity must include information on terminal observations on organ weights, gross pathology and

histopathology (full-scale) and other potential aspects related to organ and tissue toxicity to address relevant physiological systems (circulatory, digestive/excretory, endocrine, immune, integumentary, musculoskeletal, nervous, renal/urinary system, reproductive, and respiratory).

187 The sources of information provide information on haematological (i., ii., iii., and iv.) and clinical chemistry analysis (i., ii., and iii.), other potential aspects related to blood chemistry to address relevant physiological systems (circulatory digestive/excretory, endocrine, immune, musculoskeletal, and renal/urinary), terminal observations on organ weights (i., ii., and iii.), gross pathology (i., ii., iii., and iv.) and histopathology (i., ii., iii., and iv.), and other potential aspects related to organ and tissue toxicity to address relevant physiological systems (circulatory, digestive/excretory, endocrine, immune, integumentary, musculoskeletal, nervous, renal/urinary system, reproductive, and respiratory) as foreseen to be investigated in OECD TG 408.

188 However, as explained under point 1) above, these studies are affected by significant deficiencies which vitiate the information on blood chemistry, and organ and tissue toxicity that is normally investigated by the required study.

189 As a conclusion, sources of information as indicated above, provide information on repeated-dose toxicity but essential parts of information of the dangerous property are lacking (clinical signs of the relevant physiological systems, functional observations, clinical chemistry, organ weights).

190 Taken together, the relevant sources of information as indicated above, provide information on in-life observations, blood chemistry, organ and tissue toxicity. However, the reliability of these sources of information is affected by significant deficiencies.

191 Accordingly, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 408 study. Therefore, your adaptation is rejected and the information requirements is not fulfilled.

8.3. Specification of the study design

192 Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the substance is a liquid with a vapour pressure of 0.0079 Pa at 20 °C and there are no specific uses that warrant inhalation route.

193 Therefore the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance.

194 In the comments to the draft decision, you propose to adapt this standard information requirement according to Annex IX, Section 8.6.2., Column 2. You state that a sub-chronic toxicity study is not necessary since the Substance is already classified (H373).

195 Under Annex IX, Section 8.6.2., Column 2, the study may be omitted if a reliable short-term toxicity study (28 days) is available showing severe toxicity effects meeting the criteria for classifying the substance as STOT RE (category 1 or 2), for which the observed NOAEL-28 days, with the application of an appropriate uncertainty factor, allows the extrapolation towards the NOAEL-90 days for the same route of exposure.

196 As explained request 8.2, you have not provided robust study summaries which would allow verification of the reliability of the studies used, and for the reasons explained under the section on Reasons common to several requests, your category approach is rejected. Therefore, the short-term toxicity study (28-day) is not reliable.

197 In your comments to the draft decision, you also indicate that you intend to perform a sub-chronic toxicity study (90-day) on selected category members based on the results of the study performed according to the OECD TG 422 on each category member.

198 ECHA acknowledges your intentions to improve the toxicity profile of the category members and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

9. Pre-natal developmental toxicity study in one species

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

9.1. Information provided

200 You have adapted this information requirement by using weight of evidence based on the following experimental data:

(i) Teratology study in rabbits (1989) with octadecane-1-amine, EC No. 204-015-5.

9.2. Assessment of the information provided

9.2.1. Weight of evidence adaptation is rejected

201 In addition to the issues raised in the Appendix on Reasons common to several requests, ECHA has further assessed the information submitted in support of your weight of evidence adaptation and identified the following issues:

9.2.1.1. Weight of evidence cannot rely on one source of information

202 Irrespective of this deficiencies, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided source of information and found the following deficiency.

9.2.1.2. The provided study does not meet the information requirement

203 (Eco)toxicological studies must comply with a recognised test method (Art. 13(3) of REACH), in this case the OECD TG 414. Such study must cover the key parameters of the corresponding OECD test guideline (Art. 13(3) of REACH). Therefore, the following specifications must be met:

a) an exposure duration at least from implantation until one day prior to scheduled caesarean section;
b) examination of the dams for weight and histopathology of the thyroid gland, body weight of the dams, clinical signs of the dams.

204 The study i. is described as EPA regulations, TSCA (40 CFR Part 798.4700, September 1985, and revised edition May 1987). The following specifications are not according to the requirements of OECD TG 414:

a) an exposure duration of 13 days;
b) no data on examinations of dams: incidence and severity. In particular, the following investigations are missing: weight and histopathology of the thyroid gland, gravid uterus weight, uterine content, body weights, and clinical signs.

205 This study was not conducted using a recognised method. In addition, the study does not cover the above key parameters of the OECD TG 414 and this study is not an adequate basis for your read-across predictions.

206 Therefore, your adaptation is rejected and the information requirements is not fulfilled.

9.3. Specification of the study design

207 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species.

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

209 Therefore, the study must be conducted in rats or rabbits with oral administration of the Substance.

210 The Substance is a corrosive liquid and it has a classification as Skin Corr. 1B (H314). The Guidance on IRs and CSA, Section R.7.6.2.3.2. specifies that corrosive or highly irritating substances must be tested preferably via the oral route. However, testing at concentration/dose levels causing corrosivity must be avoided. Testing of neutral salts of alkaline or acidic substances is therefore more appropriate as it allows the investigation of intrinsic properties at adequate dose levels.

211 The test sample must be chosen to minimise gastrointestinal irritation and to allow investigation of intrinsic properties at adequate dose levels. This could be achieved by testing a neutralised salt of the Substance. If the PNDT study submitted in response to this decision does not deliver reliable results because of gastrointestinal irritation, further information may be considered necessary in order to investigate the intrinsic properties at adequate dose levels. If the Member State competent authorities consider that a concern must be clarified in that respect, they may decide to require further information under Substance Evaluation.

212 In your comments to the draft decision, you agree to perform the requested study. You indicate that you intend to perform a PNDT study on selected category members based on the results of the study performed according to the OECD TG 422 on each category member. ECHA understands that you do not consider the use of a neutralised form of the Substance feasible for several reasons. ECHA acknowledges your comments and reminds you to avoid corrosivity/ local irritation effects in *in vivo* studies if needed (see explanation above).

213 ECHA acknowledges your intentions to improve the toxicity profile of the category members and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

10. Long-term toxicity testing on aquatic invertebrates

214 Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

10.1. Information provided

215 You have provided:

(i) a study according to OECD TG 203 with Amines, coco alkyl with CAS RN 61788-46-3 (EC No. 262-977-1), 2002
(ii) a study according to OECD TG 201 with the category member Amines, tallow alkyl

with CAS RN 61790-33-8 (EC No. 263-125-1), 2002

(iii) a study according to OECD TG 203 with octadec-9-en-1-amine with CAS RN 112-90-3 (EC No. 204-015-5), 2002

10.2. Assessment of the information provided

10.2.1. The proposed category approach is rejected

216 For the reasons explained under the section on Reasons common to several requests, your category approach is rejected.

10.2.2. The provided studies do not meet the information requirement

217 To fulfil the information requirement, a study must comply with the OECD TG 211 and the requirements of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

218 Key parameter to be measured

a) the concentrations of the test material leading to no observed effect (NOECs) on the following parameters are estimated:
   i. the time to production of the first brood.

219 Additional requirements applicable to difficult to test substances

b) for adsorbing test chemical, dissolved total organic carbon concentrations (other than that due to the test chemical) must be maintained in all test solutions at or below 2 mg/L.

220 Reporting of the methodology and results

c) information on the test material is provided, including purity, chemical identity of impurities and identity and quantitative occurrence of the constituents.
d) the nominal test concentrations and the results of all analyses to determine the concentration of the test substance in the test vessels are reported;
e) the full record of the daily production of living offspring during the test by each parent animal is provided

221 Your registration dossier provides an OECD TG 211 studies showing the following:

222 Key parameter to be measured

a) The concentrations of the test material leading to no observed effect NOECs) were not estimated in any of the reported studies on the following parameter(s):
   i. the time to production of the first brood.

223 Additional requirements applicable to difficult to test substances

b) as already explained under Appendix 1.2., the substance is considered to be highly adsorptive. For studies ix and x. above, you report that the test was conducted with natural freshwater with a TOC content of 9.9 mg/L.

224 Reporting of the methodology and results

c) for studies i. to iii. above, you provide information on purity. However, you have provided no information on impurities or identity and quantitative occurrence of the constituents (in particular their C-chain length distribution) for any of these studies.
d) the results of all analyses to determine the concentration of the test substance in the test vessels are not reported for studies i. and ii., above.
e) the full record of the daily production of living offspring during the test by each parent animal is not provided for studies i. to iii., above.

225 Based on the above,

- all key parameters of OECD TG 211 are not covered for studies i. to iii. as you have not provided information on time to first brood.
- there are critical methodological deficiencies resulting in the rejection of the results of all studies. More specifically,
  - for studies i. to iii., the TOC content of the test medium was above the mandatory value of 2 mg/L. As already explained under Appendix 1.2., testing with high TOC test medium does not provide relevant data for the purpose of classification and labelling and PBT assessment and is therefore not acceptable.
- the reporting of studies i. to iii. is not sufficient to conduct an independent assessment of their reliability. More specifically,
  - you have not provided adequate information on the test material in any of these studies;
  - you have not reported the results of the analytical verification of exposure concentrations (studies i. and ii.) and the results of daily production of living offspring during the test (studies i. to iii.), and therefore the reliability of the study and interpretation of the results cannot be assessed.

226 Therefore, the requirements of OECD TG 211, in conjunction with OECD GD 23, are not met for any of the reported studies.

227 For all the reasons explained above, the information requirement is not fulfilled.

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

10.3. Study design and test specifications

229 OECD TG 211 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix 1.2.

11. Long-term toxicity testing on fish

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

11.1. Information provided

231 You have provided the following justification to omit the study: "Long-term test results for fish are not available. Comparing the available data on acute toxicity for fish and invertebrates indicates that additional chronic tests using fish might not contribute additional information relevant for risk assessment for aquatic ecosystems. In addition, testing of vertebrates should be avoided due to animal welfare reasons".

11.2. Assessment of the information provided

11.2.1. Your justification to omit the study has no legal basis

232 A registrant may only adapt this information requirement based on the general rules set out in Annex XI. It is noted that Column 2 of Annex IX, Section 9.1, does not allow omitting the need to submit information on long-term toxicity to fish under Column 1 (Decision of the Board of Appeal in case A-011-2018).

233 Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH.

234 Therefore, you have not demonstrated that this information can be omitted. Minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI.

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

236 In your comments to the draft decision, you indicate that you intend to perform long-term fish studies on selected category members based on the results of the studies performed according to the OECD TG 201 or 221/202/203/211 on each category member. You state that "*Based on these bridging data a new read-across/category approach will be developed which will allow to define whether and how much terrestrial studies, sediment studies and chronic fish studies are needed*".

237 ECHA acknowledges your intentions to improve the toxicity profile of the category members and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

11.3. Study design and test specifications

238 To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (Guidance on IRs and CSA, Section R.7.8.2.).

239 OECD TG 210 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix 1.2.

12. Long-term toxicity on terrestrial invertebrates

240 Short-term toxicity to invertebrates is an information requirement under Annex IX to REACH (Section 9.4.1). Long-term toxicity testing must be considered (Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

12.1. Triggering of Long-term toxicity to terrestrial invertebrates

241 Based on the information from your registration dossier, you consider the Substance to have high adsorption potential to soil by analogy to the structurally similar substance octadecylamine (EC No. 205-695-3). Furthermore, for the reasons explained under Appendix 4, you have not demonstrated that the Substance is readily biodegradable. Therefore, in the absence of soil specific data, the Substance is considered potentially highly persistent in soil.

242 On this basis information on long-term toxicity on terrestrial invertebrates must be provided.

12.2. Information provided

243 You have provided:

(i) a non-guideline study with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 2000
(ii) a study according to OECD TG 218 with C16-18-(even numbered)-alkylamines acetates (CAS 1273322-45-4).

244 The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Appendix 1.17.

13. Effects on soil micro-organisms

245 Effects on soil microorganisms is an information requirement under Annex IX to REACH (Section 9.4.2).

13.1. Information provided

246 You have provided the following justification to omit the study: "Measured data on the toxicity to soil microorganisms are not available. But read across to the quat N-(C12-14) alkyl, N-Hydroxyalkyl, N,N-dimethylammonium chloride (HYEQS) ([redacted], 2009) can be done. HYEQS has similar sorption properties when compared to the Primary alkyl amines. In the OECD 209 test of sludge respiration inhibition ([redacted], 2010a) HYEQS has a EC10 of 4 mg/L and in the OECD 216 Soil microorganism test a NOEC of > 1000 mg/kg soil dw. ([redacted], 2010a). Coco alkyl amines having a carbon distribution with a maximum at C12-C14 has a EC10 of 5.5 mg/L in the OECD 209 test (see Table 7.4.1-1). Based on these facts a NOEC of 1000 mg/kg dw. for soil micro-organisms can be justified for Coco alkyl amine in a read across approach as well. This NOEC can be used as a chronic endpoint representing detritivors (decomposers) in the terrestrial compartment".

247 ECHA understands that you predict the properties of the Substance using a read-across adaptation under Annex XI, Section 1.5. ('Grouping of substances and read-across') and that your hypothesis assumes that different compounds have the same type of effects.

13.2. Assessment of the information provided

13.2.1. The proposed read-across approach is rejected

248 Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group.

249 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

13.2.1.1. Absence of read-across documentation

250 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide a justification for the read-across including a hypothesis, explanation of the rationale for the prediction of properties and robust study summary(ies) of the study(ies) on the source substance(s) (Guidance on IRs and CSA, Section R.6.2.6.1.).

251 You have provided reference to a study conducted with another substance than the Substance in order to comply with the REACH information requirements. However, you have not provided documentation as to why this information is relevant for the Substance.

252 In the absence of such documentation, the properties of the Substance cannot be reliably predicted from the data on the source substance.

13.2.1.2. Relevance of the supporting information

253 According to the Guidance on IRs and CSA, Section R.6.2.2.1.f., "it is important to provide supporting information to strengthen the rationale for the read-across approach. Thus, in

addition to the property/endpoint being read across, it is also useful to show that additional properties, relevant to the endpoint, are also (qualitatively or quantitatively) similar between the source and target chemicals".

254 In order to support your claim that the Substance and source substance(s) have similar properties for the endpoints under consideration, you refer to Activated Sludge, Respiration Inhibition Tests for the selected analogue substance and another substance similar to the Substance (i.e. Coco alkyl amine).

255 However, these studies do not inform on effects on soil microorganisms for the Substance and of the source substance. Accordingly, this information is not considered as relevant to support your hypothesis.

13.2.1.3. Missing supporting information

256 Annex XI, Section 1.5 of the REACH Regulation states that "physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)". For this purpose, "it is important to provide supporting information to strengthen the rationale for the read-across" (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.). The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

257 Supporting information must include bridging studies to compare properties of the Substance and source substance.

258 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

259 To support the read-across you claim that the selected analogue substance has similar sorption properties and that the selected analogue substance show similar effects compared to a structurally similar substance to the Substance in studies conducted according to OECD TG 209. You have not provided any robust study summaries for the studies conducted on the analogue substance (i.e., OECD TG 209 and OECD TG 216).

260 For the source substance, you provide the study used in the prediction in the registration dossier. Apart from that study, your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data for the source substance that would confirm that both substances cause the same type of effects.

261 As explained under section 11.1.1.2., the results of Activated Sludge, Respiration Inhibition Tests do not inform on effects on soil microorganisms. Further similarity in adsorption properties is not a valid basis to demonstrate similar toxicity to soil micro-organisms. In the absence of relevant bridging studies to compare the properties of the Substance and the selected analogue substance, you have not established that they are likely to have similar properties. Therefore, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

262 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Therefore, your read-across approach under Annex XI, Section 1.5. is rejected.

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

264 In your comments to the draft decision, you indicate that you intend to perform terrestrial toxicity testing on selected category members based on the results of the studies performed according to the OECD TG 201 or 221/202/203/211 on each category member. You state that "*Based on these bridging data a new read-across/category approach will be developed which will allow to define whether and how much terrestrial studies, sediment studies and chronic fish studies are needed*".

265 ECHA acknowledges your intentions to improve the toxicity profile of the category members and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

13.3. Study design and test specifications

266 Guidance on IRs and CSA, Section R.7.11.3.1. specifies that the nitrogen transformation test (EU C.21/OECD TG 216) is considered suitable for assessing long-term adverse effects on soil microorganisms for most non-agrochemicals. As specified in EU C.21/OECD TG 216 and EU C.22/OECD TG 217, if agrochemicals (e.g., crop protection products, fertilisers, forestry chemicals) are tested, both the carbon transformation and the nitrogen transformation tests must be conducted. Your report that the substance has widespread professional use in fertilisers containing the Substance as coating agent at low concentration (< 0.1%). Therefore, despite low concentrations in fertilisers, the Substance is directly applied to soil as part of formulated agrochemicals. Therefore, information on both carbon transformation and nitrogen transformation must be provided as specified above.

14. Long-term toxicity on terrestrial plants

267 Short-term toxicity to terrestrial plants is an information requirement under Annex IX to REACH (Section 9.4.3). Long-term toxicity testing must be considered (Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

14.1. Triggering for Long-term toxicity to terrestrial plants

268 Based on the information from your registration dossier, you consider the Substance to have high adsorption potential to soil by analogy to the structurally similar substance octadecylamine (EC No. 205-695-3). Furthermore, for the reasons explained under Appendix 4, you have not demonstrated that the Substance is readily biodegradable. Therefore, in the absence of soil specific data, the Substance is considered potentially highly persistent in soil.

269 Therefore, the Substance has a high potential to adsorb to soil. On this basis information on long-term toxicity on terrestrial plants must be provided.

14.2. Information provided

270 You have provided:

(i) a study according to OECD TG 208 with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 2000

271 The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Appendix 1.18.

Reasons related to the information under Annex X of REACH

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

272 A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in a second species is an information requirement under Annex IX to REACH (Section 8.7.2., Column 2) depending on the outcome of the first PNDT study and other relevant available data.

15.1. Information provided

273 You have adapted this information requirement by using weight of evidence based on the following experimental data:

(ii) Teratology study in ras (1989) with octadecane-1-amine, EC No. 204-015-5.

15.2. Assessment of the information provided

15.2.1. Weight of evidence adaptation is rejected

274 In addition to the issues raised in the Appendix on Reasons common to several requests, ECHA has further assessed the information submitted in support of your weight of evidence adaptation and identified the following issues:

15.2.1.1. Weight of evidence cannot rely on one source of information

275 Irrespective of this deficiencies, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided source of information and found the following deficiency.

15.2.2. The provided study does not meet the information requirement

276 Toxicological studies must comply with a recognised test method (Art. 13(3) of REACH), in this case the OECD TG 414. Such study must cover the key parameters of the corresponding OECD test guideline (Art. 13(3) of REACH). Therefore, the following specifications must be met:

a) an exposure duration at least from implantation until one day prior to scheduled caesarean section;
b) examination of the dams for weight and histopathology of the thyroid gland, body weight of the dams, clinical signs of the dams.

277 The study i. is described as EPA regulations, TSCA (40 CFR Part 798.4700, September 1985, and revised edition May 1987). The following specifications are not according to the requirements of OECD TG 414:

a) an exposure duration of 10 days;
b) no data on examinations of dams: incidence and severity. In particular, the following investigations are missing: weight and histopathology of the thyroid gland, thyroid hormone measurements, gravid uterus weight, uterine content, body weights, and clinical signs.

278 This study was not conducted using a recognised method. In addition, the study does not cover the above key parameters of the OECD TG 414 and this study is not an adequate basis for your read-across predictions.

279 Therefore, your adaptation is rejected and the information requirements is not fulfilled.

15.3. Specification of the study design

280 A PNDT study according to the test method OECD TG 414 should be performed in rabbit or rat as preferred species.

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

282 Therefore, the study must be conducted in rabbits or rats with oral administration of the Substance.

283 The Substance is a corrosive liquid and it has a classification as Skin Corr. 1B (H314). The Guidance on IRs and CSA, Section R.7.6.2.3.2. specifies that corrosive or highly irritating substances must be tested preferably via the oral route. However, testing at concentration/dose levels causing corrosivity must be avoided. Testing of neutral salts of alkaline or acidic substances is therefore more appropriate as it allows the investigation of intrinsic properties at adequate dose levels.

284 The test sample must be chosen to minimise gastrointestinal irritation and to allow investigation of intrinsic properties at adequate dose levels. This could be achieved by testing a neutralised salt of the Substance. If the PNDT study submitted in response to this decision does not deliver reliable results because of gastrointestinal irritation, further information may be considered necessary in order to investigate the intrinsic properties at adequate dose levels. If the Member State competent authorities consider that a concern must be clarified in that respect, they may decide to require further information under Substance Evaluation.

285 In your comments to the draft decision, you agree to perform the requested study. You indicate that you intend to perform a PNDT study on selected category members based on the results of the study performed according to the OECD TG 422 on each category member. ECHA understands that you do not consider the use of a neutralised form of the Substance feasible for several reasons. ECHA acknowledges your comments and reminds you to avoid corrosivity/ local irritation effects in *in vivo* studies if needed (see explanation above).

286 ECHA acknowledges your intentions to improve the toxicity profile of the category members and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

16. Long-term toxicity testing on terrestrial invertebrates

287 Long-term toxicity to terrestrial invertebrates is an information requirement under Annex X to REACH (Section 9.4.4).

16.1. Information provided

288 You have provided:

(i) a study according to OECD TG 222 with Amines, hydrogenated tallow alkyl with CAS RN 61788-45-2 (EC No. 262-976-6), 2006

16.2. Assessment of the information provided

16.2.1. The proposed category approach is rejected

289 Study (i) is performed on an analogue substance. However, for the reasons explained under the section on Reasons common to several requests, your category approach is rejected.

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

291 In your comments to the draft decision, you indicate that you intend to perform terrestrial toxicity testing on selected category members based on the results of the studies performed according to the OECD TG 201 or 221/202/203/211 on each category member. You state that "*Based on these bridging data a new read-across/category approach will be developed which will allow to define whether and how much terrestrial studies, sediment studies and chronic fish studies are needed*".

292 ECHA acknowledges your intentions to improve the toxicity profile of the category members and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

16.3. Study design and test specifications

293 Guidance on IRs and CSA, Section R.7.11.3.1. specifies that the earthworm reproduction test (OECD TG 222), the Enchytraeid reproduction test (OECD TG 220), and the Collembolan reproduction test (OECD TG 232) are appropriate to cover the information requirement for long-term toxicity testing on terrestrial invertebrates. ECHA is not in a position to determine the most appropriate test protocol since this decision is dependent upon species sensitivity and substance properties. However, when log Kow >5 and log Koc >4, as in this case, the test OECD 232 is not appropriate as the dominant route of exposure for Collembolans is via pore water.

17. Long-term toxicity testing on terrestrial plants

294 Long-term toxicity to terrestrial plants is an information requirement under Annex X to REACH (Section 9.4.6).

17.1. Information provided

295 You have provided:

(i) a study according to OECD TG 208 with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 2000

17.2. Assessment of the information provided

17.2.1. The proposed category approach is rejected

296 Study (i) is performed on an analogue substance. However, for the reasons explained under the section on Reasons common to several requests, your category approach is rejected.

17.2.2. The reported study does not qualify for a long-term test

297 ISO 22030 and OECD TG 208 are both considered adequate to meet the information requirement for long-term toxicity on terrestrial plants. If a similar number of species is tested, ISO 22030 is expected to be more sensitive as it provides additional reproduction endpoints that are not covered by the OECD TG 208. However, if a higher number of species is used in the OECD 208, this test is expected to provide more relevant results in the majority of cases due to the better coverage of inter-species sensitivity. Based on a statistical analysis (Monte Carlo analysis), it was found that the OECD TG 208 can be considered of equal or greater sensitivity to the ISO 22030 when six or more species are tested. At the opposite, when fewer species are tested, the OECD TG 208 does not qualify as a long-term test due to the expected lower sensitivity when compared to the ISO 22030.

298 The study i. above was conducted with only three species.

299 Therefore, this study does not provide sufficiently broad species selection to be considered a long-term test.

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

301 In your comments to the draft decision, you indicate that you intend to perform terrestrial toxicity testing on selected category members based on the results of the studies performed according to the OECD TG 201 or 221/202/203/211 on each category member. You state that "*Based on these bridging data a new read-across/category approach will be developed which will allow to define whether and how much terrestrial studies, sediment studies and chronic fish studies are needed*".

302 ECHA acknowledges your intentions to improve the toxicity profile of the category members and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

17.3. Study design and test specifications

303 The Terrestrial Plant Test (test method: OECD TG 208) is appropriate to cover the information requirement for long-term toxicity on terrestrial plants.

304 The OECD TG 208 considers the need to select the number of test species according to relevant regulatory requirements, and the need for a reasonably broad selection of species to account for interspecies sensitivity distribution. For long-term toxicity testing, ECHA considers six species as the minimum to achieve a reasonably broad selection. Testing must be conducted with species from different families, as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD TG 208.

18. Long-term toxicity to sediment organisms

305 Long-term toxicity to sediment organisms is an information requirement under Annex X to REACH (Section 9.5.1.).

18.1. Information provided

306 You have provided:

(i) a non-guideline study with the category member Amines, tallow alkyl with CAS RN 61790-33-8 (EC No. 263-125-1), 2000
(ii) a study according to OECD TG 218 with C16-18-(even numbered)-alkylamines acetates (CAS 1273322-45-4).

18.2. Assessment of the information provided

18.2.1. The proposed category approach is rejected

307 For the reasons explained under the section on Reasons common to several requests, your category approach is rejected.

18.2.2. Tests on nematodes are not relevant to assess the toxicity of highly adsorptive test substances

308 Guidance on IRs and CSA, Section R.7.9.1. specifies that nematodes are biologically relevant species to investigate toxicity on sediment organisms. However, nematodes are selective feeders and do not ingest the sediment particles. Therefore, a justification for the

selection of the species must be provided taking into account the feeding strategy of the nematode species in connection with the binding process of the chemical to sediment particles.

309 Based on the information from your registration dossier, you conclude that all members from the PFA category are regarded as highly adsorptive to soil and sediment. You have not provided any justification as to why nematode is an adequate species to investigate the toxicity of the selected category member on sediment organisms

310 In the absence of an adequate justification, study i. above is rejected.

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

312 In your comments to the draft decision, you indicate that you intend to perform sediment toxicity testing on selected category members based on the results of the studies performed according to the OECD TG 201 or 221/202/203/211 on each category member. You state that "*Based on these bridging data a new read-across/category approach will be developed which will allow to define whether and how much terrestrial studies, sediment studies and chronic fish studies are needed*".

313 ECHA acknowledges your intentions to improve the toxicity profile of the category members and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

18.3. Study design and test specifications

314 Sediment-Water Chironomid Toxicity Test Using Spiked Sediment (test method: EU C.27/OECD TG 218) is only appropriate to cover the information requirement for long-term toxicity to sediment organisms for substances which equilibration time (time to reach steady state in the body) is not anticipated to be very long (e.g. not highly lipophilic substance such as substance with log Kow < 5 and log Koc < 3; Guidance on IRs and CSA, Section R.7.8.9.1. and R.7.8.14.2.) such as the Substance. For substances with equilibration time anticipated to be very long, the Sediment-Water Chironomid Life-Cycle Toxicity Test Using Spiked Water or Spiked Sediment (test method: EU C.40/OECD TG 233), which is an extension of the proposed test, must be conducted (Guidance on IRs and CSA, Section R.7.8.9.1. and R.7.8.14.2.). Alternatively, you may also consider conducting a Sediment-Water Lumbriculus Toxicity Test Using Spiked Sediment (test method: EU C.35/OECD TG 225). A justification must be provided as to why the chosen test method is the most appropriate and sensitive test protocol based on, for example, substance properties/uses (Guidance on IRs and CSA, Section R.7.8.9.1).

315 Guidance on IRs and CSA, Section R.7.8.10.1 specifies that spiking the water phase does not accurately represent accumulation processes within the sediment lasting longer than the test period and is only regarded as applicable to simulate pesticide spray drift event and other type of exposure (e.g. chemical spill). For industrial chemicals with continuous and intermittent release, spiking the sediment must be conducted as this approach is intended to simulate accumulated levels of substance persisting in the sediment.

316 ECHA notes that the Substance has multiple industrial uses as well as widespread professional and Consumer uses. Considering the environmental release pattern for the Substance, ECHA concludes that the study must be conducted by spiking the sediment phase.

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; (ECHA 2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).

All Guidance on REACH is available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF), ECHA (2017)
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs), ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: Procedure

The information requirement for an Extended one-generation reproductive toxicity study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the Sub-chronic toxicity study (90-day) requested in the present decision is provided; due to the fact that the results from the 90-day study is needed for the design of the EOGRTS. Similarly the information requirement for a Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) is not addressed in this decision; as the EOGRTS will cover the same parameters.

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

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 6 July 2021.

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

ECHA took into account your comments and did not amend the requests.

In the comments on the draft decision, you requested an extension of the deadline from 30 to 48 months from the date of adoption of the decision. You justified the request with the following arguments:"[…] *high level of capacity utilization at CRO level for these types to tests as indicated by several contract laboratories and evidenced by the attached letter* […]"

Based on the documentary evidence, ECHA has agreed with your request for a deadline extension.On this basis, ECHA has extended the deadline to 48 months.

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

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix 3: Addressees of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. Test methods, GLP requirements and reporting

(1) Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

(2) Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[2].

1.2. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

(1) Selection of the Test material(s)
The Test Material used to generate the new data must be selected taking into account the following:
- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.
- as explained under request 9, the test sample must be chosen to minimise gastrointestinal irritation and to allow investigation of intrinsic properties at adequate dose levels. This could be achieved by testing a neutralised salt of the Substance. When selecting a neutral salt, the potential impact of the counterion must be considered. The counterion must not have known systemic toxicity.

(2) Information on the Test Material needed in the updated dossier
- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

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

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[3].

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