~~Confidential~~

Helsinki, 13 February 2024

Addressee
Registrant as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
02 January 2014

Registered substance subject to this decision ("the Substance")
Substance name: 1,3-bis[12-hydroxy-octadecamide-N-methylene]-benzene
EC/List number: 423-300-7

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 information under request 1, 2, 3 and 11 below by ***20 May 2025*** and all other information listed below by ***20 May 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: Bacterial reverse mutation test, OECD TG 471).

2. Long-term toxicity testing on aquatic invertebrates, also requested below (triggered by Annex VII, Section 9.1.1., Column 2; test method: EU C.20./OECD TG 211).

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

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

4. *In vitro* micronucleus study (Annex VIII, Section 8.4.2., test method: OECD TG 487). The aneugenic potential of the Substance must be assessed with an additional control group for aneugenicity on top of the control group for clastogenicity, if the Substance induces an increase in the frequency of micronuclei.

5. Only if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained, *in vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: EU B.17./OECD TG 476 or EU B.67./OECD TG 490).

6. Justification for an adaptation of the short-term repeated dose toxicity study (28 days) (Annex VIII, Section 8.6.1., Column 2) based on the request 9 below.

   If the sub-chronic toxicity study (90 days) is not requested:

   Short-term repeated dose toxicity (28 days) (Annex VIII, Section 8.6.1.) by oral route, in rats, to be combined with the screening for reproductive/developmental toxicity requested below.

7. Screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats.

8. Long-term toxicity testing on fish, also requested below (triggered by Annex VIII, Section 9.1.3., Column 2).

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

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

10. 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).

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

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

13. Soil simulation testing (Annex IX, Section 9.2.1.3.; test method: EU C.23/OECD TG 307) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.

14. Sediment simulation testing (Annex IX, Section 9.2.1.4.; test method: EU C.24/OECD TG 308) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.

15. Identification of degradation products (Annex IX, Section 9.2.3.; test method: EU C.23/OECD TG 307 and EU C.24/OECD TG 308).

16. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2; test method: EU C.13/OECD TG 305), aqueous or dietary exposure.

17. Long-term toxicity testing on terrestrial invertebrates (triggered by Annex IX, Section 9.4.1., Column 2; test method: OECD TG 222 or OECD TG 220 or OECD TG 232)

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

19. Long-term toxicity on terrestrial plants (triggered by Annex IX, Section 9.4.3., Column 2; test method: EU C.31./OECD TG 208 with at least six species or ISO 22030)

The reasons for the requests 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 addressee of the decision and its

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.

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 request(s)
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 request(s)

Reasons common to several requests

1 You have provided experimental data for the following standard information requirements:

- 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.)
- Short-term repeated dose toxicity (28 days) (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Sub-chronic toxicity study (90 days) (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

2 ECHA has identified the common deficiency addressed below.

0.1. Experimental data rejected because the identity of the test material is unclear

3 To comply with an information requirement, the test material in a study must be representative for the Substance (Article 10 and Recital 19 of REACH; Guidance on IRs and CSA, Section R.4.1).

4 The provided study has been conducted with a test material referred to as 'AMIDE#71', EC 423-300-7. In your dossier, you state the following:

- you consider that 'AMIDE#71' is "*not identical*" to the Substance as it is a multi-constituent and not a UVCB;
- The two main constituents of 'AMIDE#71' are the same as those of the Substance (i.e., CAS numbers 128554-52-9 and 1262779-46-3)
- You state that "*a number of impurities were also present in AMIDE#71* […] *(some identified and some unknown) plus residual starting products, which are considered to be very similar or identical in some cases, to the other constituents of* [the Substance]."

5 Based on the above, ECHA understands that the test material use may differ from the Substance. However, in the absence of a comprehensive description of the test material composition (including quantitative information), ECHA is not in a position to assess those compositional differences. Therefore, you have not demonstrated that it is representative for the Substance.

6 Based on the above, the provided experimental data is not adequate to fulfil the respective information requirements.

Reasons related to the information under Annex VII of REACH

1. *In vitro* gene mutation study in bacteria

7 An in vitro gene mutation study in bacteria is an information requirement under Annex VII, Section 8.4.1.

1.1. Information provided

8 You have provided an *in vitro* gene mutation study in bacteria (2013) with the Substance.

1.2. Assessment of the information provided

1.2.1. Unclear test material

9 As explained in Section 0.1., you have not provided adequate information to confirm that the test material used to conduct the provided study is representative of the Substance. In addition, ECHA identified the endpoint-specific issue addressed below.

1.2.2. The provided study does not meet the specifications of the test guideline

10 To fulfil the information requirement, a study must comply with OECD TG 471 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the test is 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) at least 5 doses are evaluated, in each test condition;

c) triplicate plating is used at each dose level;

d) concurrent strain-specific positive controls, both with and without metabolic activation, are included in each assay and the number of revertant colonies per plate induced by the positive controls demonstrates the effective performance of the assay;

e) a concurrent negative control is included in each assay and the number of revertant colonies per plate for the concurrent negative control is inside the historical control range of the laboratory;

f) the mean number of revertant colonies per plate is reported for the treated doses and the controls;

g) negative results are confirmed in a repeat experiment with modification of study parameters to extend the range of conditions assessed, or a justification why confirmation of negative results is not considered necessary is provided.

11 In the provided study:

a) the test was performed with the strains S. typhimurium TA 1535, TA 1537, TA 98 and TA 100 (i.e., the strain *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) is missing);

b) it is unclear how many doses were evaluated in absence and in presence of metabolic activation since you only reported a range (i.e., 3 - 333 µg/plate);

c) triplicate plating was not used at each dose level;

d) concurrent strain-specific positive controls were not reported to be included in the study;

e) a concurrent negative control was not included in the study and it was not reported if the number of revertant colonies per plate for the concurrent negative control was inside the historical control range of the laboratory;

f) the mean number of revertant colonies per plate for the treated doses and the controls was not reported;

g) no repeat experiment was performed to confirm the negative results and no justification was provided.

12 The information provided does not cover the specification(s) required by the OECD TG 471.

13 Therefore, the information requirement is not fulfilled.

2. Long-term toxicity testing on aquatic invertebrates

14 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII, Column 1, Section 9.1.1. However, under Column 2, long-term toxicity testing on aquatic invertebrates may be required by the Agency if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

2.1. Triggering of the information requirement

15 In the provided study according to EU Method A.6 (2013), the saturation concentration of the Substance in water was determined to be < 0.64 mg/L at 20°C.

16 Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates must be provided.

2.2. Information requirement not fulfilled

17 The information provided, its assessment and the specifications of the study design are addressed under request 11.

3. Growth inhibition study aquatic plants

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

3.1. Information provided

19 You have provided a Growth inhibition study on aquatic plants/algae (2013) based on EU Method C.3 with the Substance.

3.2. Assessment of the information provided

3.2.1. Unclear test material

20 As explained in Section 0.1., you have not provided adequate information to confirm that the test material used to conduct the provided study is representative of the Substance. In addition, ECHA identified the endpoint-specific issue addressed below.

3.2.2. The provided study does not meet the specifications of the test guideline

21 To fulfil the information requirement, a study must comply with OECD TG 201 and the specifications of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). The Substance is difficult to test as it has low solubility (< 0.64 mg/L) and high adsorptive properties (Log K_{ow} > 6.5 and Log K_{oc} > 5.63). Therefore, the following specifications must be met:

Technical specifications impacting the sensitivity/reliability of the test

a) the test concentrations are below the limit of solubility of the test material in the dilution water;

Additional requirements applicable to difficult to test substances

b) if the test material is tested at the saturation concentration, evidence must be provided that all reasonable efforts have been taken to achieve a saturation concentration, which include:

1) an analytical method validation report demonstrating that the analytical method is appropriate, and

2) information on the saturation concentrations of the test material in water and in the test solution, and

3) a description of the method used to prepare the test solution, and

4) the results of a preliminary experiment demonstrating that the test solution preparation method is adequate to maximize the concentration of the test material in solution;

Reporting of the methodology and results

c) the test design is reported (*e.g.*, number of replicates, number of test concentrations);

d) the test conditions are reported (*e.g.*, composition of the test medium);

e) the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported. Algal biomass is normally determined based on dry weight per volume, or alternatively as cell counts or biovolume using microscopy or an electric particle counter. If an alternative method is used (e.g. flow cytometry, *in vitro* or *in vivo* fluorescence, or optical density), a satisfactory correlation with biomass must be demonstrated over the range of biomass occurring in the test;

f) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;

g) the results of the analytical determination of exposure concentrations are provided.

22 In the provided study :

Technical specifications impacting the sensitivity/reliability of the test

a) the test concentrations ranged from 10 to 100 mg/L and your report in your dossier a limit of solubility of the test material in water < 0.64 mg/L;

Additional requirements applicable to difficult to test substances

b) the test material is a UVCB and was tested at above its saturation concentration and:

1) you have not provided an analytical method validation report demonstrating that the analytical method (TOC) is appropriate considering the

requirements specified under Section 3.3 below;

2) you have provided only an unbounded water solubility estimate for the Substance which does not inform on the range of solubility of its constituents. Furthermore, you have provided no information on the solubility limit of the Substance in the test solution;

3) you explain that test solutions were prepared from a homogeneous dispersion in deionised water and that the test solutions treated with ultra-sonic waves. However, you have not described in detail how the test solutions were prepared (e.g., duration and intensity of ultrasonic treatment, procedure to remove undissolved particles);

4) you have not provided the results of a preliminary experiment demonstrating that the test solution preparation method was adequate to maximize the concentration of the test material in solution;

Reporting of the methodology and results

c) on the test design, you have not specified the number of replicates and the number of test concentrations;

d) on the test conditions, you have not specified the composition of the test medium;

e) the method used to determine algal biomass is not reported;

f) tabulated data on the algal biomass determined daily for each treatment group and control are not reported;

g) the results of the analytically determined exposure concentrations are not provided;

23 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the test was conducted at concentrations that are well above the expected water solubility limit of the Substance in the test media;
- the Substance is difficult to test and you have not provided adequate justification that the test procedure was adequate to investigate the intrinsic properties of the test material;
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, key elements of the test design and test procedure are missing. Therefore, compliance with the specifications of the OECD TG 201 / EU Method C.3 cannot be assessed. In the absence of tabulated data on the algal biomass, ECHA cannot conduct an independent assessment as to whether the validity criteria of the test guideline were met. Finally, as you have not provided adequate information on the analytical method and on the results of the analytical verification of exposure, ECHA cannot assess whether exposure was satisfactorily maintained over the exposure phase and the interpretation of the results of the study.

24 On this basis, the specifications of OECD TG 201 are not met.

25 Therefore, the information requirement is not fulfilled.

3.3. Study design

26 The Substance is difficult to test due to the low solubility (< 0.64 mg/L) and high adsorptive properties (Log K_{ow} > 6.5 and Log K_{oc} > 5.63). OECD TG 201 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 201. 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.

27 For multi-constituents/UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key constituents or groups of constituents).

28 If you decide to use the Water Accommodated Fraction (WAF) approach, in addition to the above, you must:

- provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any remaining non-dissolved test material including a justification for the separation technique);
- prepare WAFs separately for each dose level (i.e. loading rate) and in a consistent manner.

Reasons related to the information under Annex VIII of REACH

4. *In vitro* micronucleus study

29 An in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study is an information requirement under Annex VIII, Section 8.4.2.

4.1. Information provided

30 You have provided an *in vitro* chromosome aberration study in mammalian cells (2013) with the Substance.

4.2. Assessment of the information provided

4.2.1. Unclear test material

31 As explained in Section 0.1., you have not provided adequate information to confirm that the test material used to conduct the provided study is representative of the Substance. In addition, ECHA identified the endpoint-specific issue addressed below.

4.2.2. The provided study does not meet the specifications of the test guideline

32 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. The study must comply with the OECD TG 473 or the OECD TG 487, respectively (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the maximum concentration tested induces 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 corresponds to 10 mM, 2 mg/mL or 2 µL/mL, whichever is the lowest;

b) at least 3 concentrations are evaluated, in absence and in presence of metabolic activation;

c) at least 300 well-spread metaphases are scored per concentration;

d) one positive control is included in the study;

e) the negative control data is ideally within the 95% control limits of the distribution of the laboratory's historical negative control database;

f) data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures is reported;

g) to conclude on a negative outcome, a negative response is obtained in all three experimental conditions described in paragraph 28 of OECD TG 473, using a short-term treatment with and without metabolic activation and long-term treatment without metabolic activation.

33 In the provided study:

a) the maximum tested concentration did not induce 55+5% of cytotoxicity compared to the negative control, and it did not induce the precipitation of the tested substance, and it was less than 10 mM, 2 mg/mL or 2 µL/mL;

b) it is unclear how many doses were evaluated since you only reported a concentration range (i.e., 1 - 10 µg/ml) in absence and in presence of metabolic activation;

c) you did not report the number of metaphases scored per concentration;

d) no positive control was included in the study;

e) you did not report if the negative control did show a response within the historical control range of the laboratory;

f) data on the cytotoxicity and/or the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures were not reported;

g) one of three experimental conditions described in paragraph 28 of OECD TG 473 (i.e. a short-term treatment without metabolic activation is missing to conclude on a negative outcome.

34 The information provided does not cover the specifications(s) required by the OECD TG 473.

35 Therefore, the information requirement is not fulfilled.

4.3. Study design

36 According to the Guidance on IR & CSA, Section R.7.7.6.3., either the in vitro mammalian chromosomal aberration ("CA") test (test method OECD TG 473) or the in vitro mammalian cell micronucleus ("MN") test (test method OECD TG 487) can be used to investigate chromosomal aberrations in vitro. However, while the MN test detects both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the CA test detects only clastogenicity, as OECD TG 473 is not designed to measure aneuploidy (see OECD TG 473, paragraph 2). Therefore, you must perform the MN test (test method OECD TG 487), as it enables a more comprehensive investigation of the chromosome damaging potential in vitro. Moreover, in order to demonstrate the ability of the study to identify clastogens and aneugens, you must include two concurrent positive controls, one known clastogen and one known aneugen [1] (OECD TG 487, paragraphs 33 to 35).

4.3.1. Assessment of aneugenicity potential

37 If the result of the MN test is positive, i.e. your Substance induces an increase in the frequency of micronuclei, you must assess the aneugenic potential of the Substance.

38 In line with the OECD TG 487 (paragraph 4), you should use one of the centromere labelling or hybridisation procedures to determine whether the increase in the number of micronuclei is the result of clastogenic events (i.e. micronuclei contain chromosome fragment(s)) and/or aneugenic events (i.e. micronuclei contain whole chromosome(s)).

[1] According to the TG 487 (2016) "At the present time, no aneugens are known that require metabolic activation for their genotoxic activity" (paragraph 34).

5. *In vitro* gene mutation study in mammalian cells

39 An in vitro gene mutation study in mammalian cells is an information requirement under Annex VIII, 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.

5.1. Triggering of the information requirement

40 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.

41 The information for the in vitro gene mutation study in bacteria and for the in vitro cytogenicity study in mammalian cells or in vitro micronucleus study provided in the dossier are rejected for the reasons provided in requests 1 and 4.

42 The result of the requests for an in vitro gene mutation study in bacteria and for an in vitro micronucleus study 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.

43 Consequently, you are required to provide information for this information requirement, if the in vitro gene mutation study in bacteria and the in vitro micronucleus study provides a negative result.

5.2. Information provided

44 You have adapted this information requirement by using Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from the following substance:

(i) an *in vitro* gene mutation study in mammalian cells (2011) with the source substance EA-3098; [redacted] (polyamide), EC 434-430-9.

45 You provide a read-across justification document in IUCLID CSR.

46 You provide the following reasoning for the prediction of this information requirement: "*This substance is a multi-constituent composed of three constituents, all of which are structurally similar to the constituents of MXDA bisamide*" and "*The molecular weights (664, 681, 962) are comparable to those of the MXDA polyamide constituents*".

47 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

5.3. Assessment of the information provided

5.3.1. Read-across adaptation rejected

48 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.

49 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).

5.3.1.1. Missing characterisation of the group members

50 Annex XI, Section 1.5. 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 group*."

51 Therefore, qualitative and quantitative information on the compositions of the Substance and of the source substance must be provided to allow assessing whether the attempted predictions are compromised by the composition and/or impurities.

52 In your read-across justification you indicate that the source substance is a multi-constituent substance. You report that the source substance is composed of three

constituents, all of which are structurally similar to the constituents of MXDA bisamide (the Substance). You do not inform on the identity of the constituents or whether there are any impurities which may constitute the remaining of the composition of the source substance.

53 Without this information, no qualitative or quantitative comparative assessment of the compositions of the Substance and of the source substance can be completed. Therefore, it is not possible to assess whether the attempted predictions are compromised by the composition of the source substance.

5.3.1.2. Inadequate read-across hypothesis

54 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 include an explanation why the properties of the Substance may be predicted from other substances in the group, i.e. a read-across hypothesis. This hypothesis should be based on recognition of the structural similarities and differences between the substances (Guidance on IRs and CSA, Section R.6.). It should explain why the differences in the chemical structures should not influence the toxicological properties or should do so in a regular pattern, taking into account that variations in chemical structure can affect both toxicokinetics (uptake and bioavailability) and toxicodynamics (e.g. interactions with receptors and enzymes) of substances (Guidance on IRs and CSA, Section R.6.2.1.3).

55 Your read-across hypothesis is only based on the structural similarity between the Substance and the source substance, which you consider a sufficient basis for predicting the properties of the Substance. However, your hypothesis does not explain why the structural differences between the substances do not influence the toxicological properties or do so in a regular pattern.

56 While structural similarity is a prerequisite for applying the grouping and read-across approach, it does not necessarily lead to predictable or similar toxicological properties. You have not provided a well-founded hypothesis to establish a reliable prediction for toxicological property, explaining why the structural differences do not influence toxicokinetics and toxicodynamics of the substances, and thus why the properties of the Substance may be predicted from information on the source substance.

5.3.1.3. Missing supporting information to compare properties of the substances

57 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 supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance(s) (Guidance on IRs and CSA R.6., Section R.6.2.2.1.f.).

58 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar source substance causes the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the source substance is necessary to confirm that the 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).

59 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 Substance that would confirm that both substances cause the same type of effects.

60 In the absence of such information, you have not established that the Substance and the source substance are likely to have similar properties. Therefore you have not provided sufficient supporting information to scientifically justify the read-across.

5.3.1.4. Missing information on the identity of the test material

61 Under Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment.

62 In order to predict the properties of the Substance, the test material used in the study on the source substance must be representative for the source substance (Article 10 and Recital 19 of REACH; Guidance on IRs and CSA, Section R.4.1.). Therefore, the unambiguous characterisation of the composition of the test material used to generate the source data is required to assess whether the test material is representative for the source substance.

63 You have identified the test material as EA-3098; [redacted] (polyamide), without further information, including composition of the test material.

64 In the absence of the information on the composition of the test material (including qualitative and quantitative information on impurities), you have not demonstrated that the test material is representative for the source substance. Therefore, the study is not adequate for the purpose of classification and labelling and/or risk assessment.

65 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance. On this basis, your read-across approach under Annex XI, Section 1.5. is rejected.

66 Therefore, the information requirement is not fulfilled.

5.4. Study design

67 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.

6. Short-term repeated dose toxicity (28 days)

68 A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII, Section 8.6.1. This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 or a general adaptation rule under Annex XI.

6.1. Information provided

69 You have provided a sub-acute toxicity study (2013) with the Substance.

6.2. Assessment of the information provided

6.2.1. Unclear test material

70 As explained in Section 0.1., you have not provided adequate information to confirm that the test material used to conduct the provided study is representative of the Substance.

71 Therefore, the information requirement is not fulfilled.

6.3. Study design

72 When there is no information available neither for the 28-day repeated dose toxicity (EU B.7, OECD TG 407), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

73 The study design is addressed in request 7.

6.3.1. Justification for an adaptation of the short-term repeated dose toxicity study (Annex VIII, Section 8.6.1., Column 2)

74 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 9).

75 According to Annex VIII, Section 8.6.1., Column 2 and to prevent unnecessary animal testing, a short-term toxicity study (28 days) does not need to be conducted. Therefore, to comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to provide a justification for adaptation, as provided in Annex VIII, Section 8.6.1., Column 2.

76 In case the adopted decision no longer contains a request for a 90-day study, you are required to provide a 28-day study.

77 Therefore, you are requested to either submit:

- a justification for the adaptation according to Annex VIII, Section 8.6.1., Column 2, based on request 9; or
- a 28-day study as per the study design described in 6.3 in case the 90-day study is not requested in the adopted decision.

7. Screening study for reproductive/developmental toxicity

78 A screening study for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1.

7.1. Information provided

79 You have adapted this information requirement by using Annex VIII, Section 8.7.1., Column 2. To support the adaptation, you have provided the following information:

(i) A prenatal developmental toxicity study in rat (2009) with the Substance.

7.2. Assessment of the information provided

7.2.1. Unclear test material

80 As explained in Section 0.1., you have not provided adequate information to confirm that the test material used to conduct the provided study is representative of the Substance.

81 Based on the above, your adaptation is rejected.

82 Therefore, the information requirement is not fulfilled.

7.3. Study design

83 A study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed in rats.

84 As the Substance is a solid, the study must be conducted with oral administration of the Substance (Annex VIII, Section 8.7.1., Column 1).

85 Therefore, the study must be conducted in rats with oral administration of the Substance.

86 In case the adopted decision no longer contains a request for a sub-chronic (90 days) study (e.g. as a result of an overall tonnage band change of the joint submission), a screening study for reproductive/developmental toxicity performed according to the OECD TG 422 is preferred.

8. Long-term toxicity testing on fish

87 Short-term toxicity testing on fish is an information requirement under Annex VIII, Column 1, Section 9.1.3. However, long-term toxicity testing on fish may be required by the Agency (Section 9.1.3., Column 2) if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

8.1. Triggering of the information requirement

88 As already explained in request 2, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

8.2. Information requirement not fulfilled

89 The information provided, its assessment and the specifications of the study design are addressed under request 12.

Reasons related to the information under Annex IX of REACH

9. Sub-chronic toxicity study (90 days)

90 A sub-chronic toxicity study (90 days) is an information requirement under Annex IX, Section 8.6.2.

9.1. Information provided

91 You have provided a sub-chronic toxicity study (2007) with the Substance.

9.2. Assessment of the information provided

9.2.1. Unclear test material

92 As explained in Section 0.1., you have not provided adequate information to confirm that the test material used to conduct the provided study is representative of the Substance. In addition, ECHA identified the endpoint-specific issue addressed below.

9.2.2. The provided study does not meet the specifications of the test guideline

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

a) the highest dose level should aim to induce toxicity or reach the limit dose;

b) the oestrus cycle in females is examined at necropsy.

94 In the provided study:

a) the highest dose level tested was 250 mg/kg bw/day, which is below the limit dose of OECD TG 408, and no adverse effects were observed;

b) oestrus cyclicity was not assessed.

95 The information provided does not cover the specification(s) required by the OECD TG 408.

96 Therefore, the information requirement is not fulfilled.

9.3. Study design

97 Following the criteria provided in Annex IX, Section 8.6.2., Column 2, and considering the Guidance on IRs and CSA, Section R.7.5.6.3.2., the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance.

98 According to the OECD TG 408, the rat is the preferred species.

99 Therefore, the study must be performed in rats according to the OECD TG 408 with oral administration of the Substance.

10. Pre-natal developmental toxicity study in one species

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

10.1. Information provided

101 You have provided a pre-natal developmental toxicity study in rats (2009) with the Substance.

10.2. Assessment of the information provided

10.2.1. Unclear test material

102 As explained in Section 0.1., you have not provided adequate information to confirm that the test material used to conduct the provided study is representative of the Substance.

103 Therefore, the information requirement is not fulfilled.

10.3. Study design

104 A PNDT study according to the test method OECD TG 414 should be performed in rats or rabbits as preferred species.

105 As the Substance is a solid, the study must be conducted with oral administration of the Substance (Annex IX, Section 8.7.2., Column 1).

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

11. Long-term toxicity testing on aquatic invertebrates

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

11.1. Information provided

108 You have adapted this information requirement and provided the following justification:

(i) "*The substances is classified for the environment as Chronic Category 4 (May cause long lasting harmful effects to aquatic life).* […]. *Results of acute testing in fish, daphnia and algae showed no toxic effects at the limit of the substances water solubility* […] *If considered as a chronic endpoint, a NOEC of 10 mg/l […] from an algal inhibition study indicates that the substance may not have any concern for long-term toxicity* […]. *The derived PNECs from the acute studies are considered as not being fully reliable for a comparison against PEC to indicate whether long-term testing is required.* […] *an assessment of the substance constituents bioaccumulation potential indicates that bioaccumulation is not anticipated to be significant for the substance and that the substance may not be readily bioavailable to aquatic organisms.* […] *the concentration of substance in water is anticipated to be at levels were significant toxicity should not occur. Based on the above a long-term daphnia study is not proposed*".

11.2. Assessment of the information provided

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

109 A registrant may only adapt this information requirement based on the general rules set out in Annex XI.

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

111 Therefore, you have not demonstrated that this information can be omitted and the information requirement is not fulfilled.

11.1. Study design

112 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 request 3.

12. Long-term toxicity testing on fish

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

12.1. Information provided

114 You have adapted this information requirement and provided the following justification:

(i) "*The substances is classified for the environment as Chronic Category 4 (May cause long lasting harmful effects to aquatic life).* […]. *Results of acute testing in fish, daphnia and algae showed no toxic effects at the limit of the substances water solubility* […] *If considered as a chronic endpoint, a NOEC of 10 mg/l […] from an algal inhibition study indicates that the substance may not have any concern for long-term toxicity* […]. *The derived PNECs from the acute studies are considered as not being fully reliable for a comparison against PEC to indicate whether long-term testing is required.* […] *an assessment of the substance constituents bioaccumulation potential indicates that bioaccumulation is not anticipated to be significant for the substance and that the substance may not be readily bioavailable to aquatic organisms.* […] *the concentration of substance in water is anticipated to be at levels were significant toxicity should not occur. Based on the above a long-term fish study is not proposed*".

12.2. Assessment of the information provided

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

115 A registrant may only adapt this information requirement based on the general rules set out in Annex XI.

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

117 Therefore, you have not demonstrated that this information can be omitted and the information requirement is not fulfilled.

12.1. Study design

118 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.).

119 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 request 3.

13. Soil simulation testing

120 Soil simulation testing is an information requirement under Annex IX to REACH (Section 9.2.1.3.) for substances with a high potential for adsorption to soil.

13.1. Triggering of the information requirement

121 A high potential for adsorption is indicated by lipophilicity e.g. when log K_{ow} > 4, log $K_{oc,soil}$ > 4 (Guidance on IRs and CSA R.7.9.4.3) or other mechanisms than driven by the lipophilicity e.g. ionising substances (at pH 4-9), surface active substances, substances that bind chemically with soil components.

122 The Substance has a high partition coefficient based on log K_{ow} > 6.5 and high adsorption coefficient based on log K_{oc} > 5.63 and therefore has high potential for adsorption to soil.

13.2. Information provided

123 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.2.1.3. To support the adaptation, you have provided the following justification:

(i) "*Direct exposure of soil is considered unlikely from use. If the substance is released to water, Indirect exposure of soil cannot be discounted based on the physico-chemical properties of the substance (log Pow, log Koc) which indicate that the substance may partition into the terrestrial compartment from water and has potential to adsorb to soil particles and accumulate in the terrestrial compartment*."

124 You also provide the following justification to omit the study:

(ii) "*due to the very limited degradation observed in ready biodegradation tests and the known lack of degradation of this substance type, it is considered that further soil simulation testing would not provide any additional useful experimental data to further assess the environmental fate of the substance*".

13.3. Assessment of the information provided

13.3.1. The provided adaptation does not meet the criteria of Annex IX, Section 9.2.1.3., Column 2 (justification (i) above)

125 Under Annex IX, Section 9.2.1.3., Column 2, the study may be omitted if direct and indirect exposure to soil is unlikely. The requirements for absence of direct and indirect exposure to soil must be met for all uses throughout the life-cycle including the waste stage (Guidance on IRs and CSA, R.5).

126 In section 3.5 of your registration dossier, you report industrial and professional uses with the following environmental release categories (ERCs):

- ERC 4 - Use of non-reactive processing aid at industrial site (no inclusion into or onto article)
- ERC5 - Use at industrial site leading to inclusion into/onto article
- ERC8a - Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor)
- ERC8c - Widespread use leading to inclusion into/onto article (indoor)
- ERC8d - Widespread use of non-reactive processing aid (no inclusion into or onto article, outdoor)
- ERC8f - Widespread use leading to inclusion into/onto article (outdoor)

127 You report that some of the Substance uses lead to inclusion into/onto article but you have provided no information on article service life.

128 The industrial and professional uses reported in your technical dossier are expected to lead to release to the environment. For instance, the reported ERCs have default emission

factors to water (before STP) ranging from 5 to 100%. Furthermore, ERC 4, 5 and 8d and 8f have default emission factors to soil of 5%, 1%, 20% and 0.5%, respectively. ECHA notes that you have not provided a quantitative exposure assessment for soil in your CSR.

129 Therefore, exposure to the soil compartment may occur. Furthermore, indirect exposure through spreading of sewage sludge on land cannot be excluded. Finally, you have not included any information on articles service life for the Substance.

130 On this basis, you have not demonstrated that exposure to soil is unlikely and your adaption is rejected.

13.3.1. Your justification to omit the study has no legal basis (justification (ii) above)

131 A registrant may only adapt this information requirement based on the general rules set out in Annex XI or the specific rules set out in Annex IX, Section 9.2.1.3., Column 2.

132 Your justification under point (ii) above to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH or Annex IX, Section 9.2.1.3., Column 2 and the legal basis you are relying on for your intended adaptation is not apparent to ECHA.

133 Therefore, you have not demonstrated that this information can be omitted.

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

13.4. Study design

135 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1):

(1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and

(2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

136 In accordance with the specifications of OECD TG 307, you must perform the test using at least four soils representing a range of relevant soils (i.e. varying in their organic content, pH, clay content and microbial biomass).

137 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 307.

138 In accordance with the specifications of OECD TG 307, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents (Guidance on IRs and CSA, Section R.7.9.4.1.). By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

139 Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the

study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 307; Guidance on IRs and CSA, Section R.11.4.1.).

14. Sediment simulation testing

140 Sediment simulation testing is an information requirement under Annex IX to REACH (Section 9.2.1.4.) for substances with a high potential for adsorption to sediment.

14.1. Triggering of the information requirement

141 A high potential for adsorption is indicated by lipophilicity e.g. when log K_{ow} >4, log $K_{oc,sediment}$ >4 (Guidance on IRs and CSA R.7.9.4.3) or by other mechanisms than driven by the lipophilicity e.g. ionising substances (at pH 4-9), surface active substances, substances that bind chemically with sediment components.

142 The Substance has a high partition coefficient based on log K_{ow} > 6.5 and high adsorption coefficient based on log K_{oc} > 5.63 and therefore has high potential for adsorption to sediment.

14.2. Information provided

143 You have adapted this information requirement and provided the following justification:

(i) "*If the substance is released to water, Indirect exposure of sediment cannot be discounted based on the physico-chemical properties of the substance (log Pow, log Koc) which indicate that the substance may partition into the sediment compartment from water and has potential to adsorb to sediment and accumulate in sediment. However, due to the very limited degradation observed in ready biodegradation tests and the known lack of degradation of this substance type, it is considered that further sediment simulation testing would not provide any additional useful experimental data to further assess the environmental fate of the substance*."

14.3. Assessment of the information provided

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

144 A registrant may only adapt this information requirement based on the general rules set out in Annex XI or the specific rules set out in Annex IX, Section 9.2.1.4., Column 2.

145 Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH or Annex IX, Section 9.2.1.4., Column 2 and the legal basis you are relying on for your intended adaptation is not apparent to ECHA.

146 Therefore, you have not demonstrated that this information can be omitted.

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

14.4. Study design

148 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

(1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and

(2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

149 In accordance with the specifications of OECD TG 308, you must perform the test using two sediments. One sediment should have a high organic carbon content (2.5-7.5%) and a fine texture, the other sediment should have a low organic carbon content (0.5-2.5%) and a coarse texture. If the Substance may also reach marine waters, at least one of the water-sediment systems should be of marine origin.

150 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 308.

151 In accordance with the specifications of OECD TG 308, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents (Guidance on IRs and CSA, Section R.7.9.4.1.). By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

152 Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 308; Guidance on IRs and CSA, Section R.11.4.1.).

15. Identification of degradation products

153 Identification of abiotic and biotic degradation products is an information requirement under Annex IX to REACH (Section 9.2.3.).

154 You have not submitted any information for this requirement.

155 Therefore, the information requirement is not fulfilled.

15.1. Study design

156 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

(1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and

(2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

157 Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported. In addition, identified transformation/degradation products must be considered in the CSA including PBT assessment.

158 You must obtain this information from the degradation studies requested in requests 13 and 14.

159 To determine the degradation rate of the Substance, the requested studies according to OECD TG 308 and 307 (requests 13 and 14) must be conducted at 12°C and at (a) test material application rate(s) reflecting realistic assumptions. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline) and at higher application rate (e.g. 10 times).

16. Bioaccumulation in aquatic species

160 Bioaccumulation in aquatic species is an information requirement under Annex IX to REACH (Section 9.3.2.).

16.1. Information provided

161 You have adapted this information requirement by using Annex XI, Section 2. (testing is technically not possible). To support the adaptation, you have provided the following information:

(i) a justification as to why testing is technically not possible;

162 In addition, you have adapted this information requirement by using Annex XI, Section 1.3. (Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs). To support the adaptation, you have provided the following information:

(ii) predictions from the regression method of BCFwin (v 2.17).

16.2. Assessment of the information provided

16.2.1. Testing not technically possible adaptation rejected

163 According to Annex XI, Section 2., a study may be omitted if it is technically not feasible to conduct because of the properties of the substance. The guidance given in the test methods referred to in Article 13(3), in this case OECD TG 305, more specifically on the technical limitations of a specific method, shall always be respected.

164 The OECD TG 305 provides in particular that this test is applicable to water-soluble and poorly water-soluble compounds. As regards to water solubility, no lower limit is specified under which the study would be not feasible.

165 You claim that, due to the Substance low solubility (< 0.64 mg/L) and strong sorbing properties (based on log Koc >5.63), an OECD Guideline 305 study is considered to be unfeasible to conduct. You did not provide any experimental evidence to support your claim.

166 Furthermore, you state that, as the substance is a complex UVCB, it is not expected that an OECD 305 study would be able to accurately determine which components were responsible for different BCFs. However, you did not provide any justification as to why the approaches described in Appendix 4, Section 2.1 would not allow generating information on the Substance.

167 Your claim does not take into account the specific technical limitations, or lack thereof, of the applicable test method.

168 Based on the above, your adaptation is rejected.

16.2.2. (Q)SAR adaptation rejected

169 Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

(1) the prediction needs to be derived from a scientifically valid model,

(2) the substance must fall within the applicability domain of the model,

(3) results need to be adequate for the purpose of risk assessment or classification and labelling, and

(4) adequate and reliable documentation of the method must be provided.

16.2.2.1. The prediction does not cover all constituents of the Substance

170 Under ECHA Guidance R.6.1.7.3. a prediction is adequate for the purpose of classification and labelling and/or risk assessment if the following cumulative conditions are met:

- the composition of the substance is clearly defined, and
- different constituents of the same substance are predicted individually.

171 Your registration dossier provides the following information:

- In Section 1.1. of your technical dossier, you define the Substance as a UVCB
- In Section 1.2., you indicate the following constituents in the composition of your Substance:
  - N-(3-(aminomethyl)benzyl)-12-hydroxyoctadecanamide
  - 12-hydroxyoctadecanoic acid
  - 9, 10-dihydroxy-N-(3-((12-hydroxyoctadecanamido)methyl)benzyl)octadecanamide
  - N,N'-(1,3-phenylenebis(methylene))bis(12-hydroxyoctadecanamide)
  - N-(3-((9, 10-dihydroxyoctadecanamido)methyl)benzyl)icosanamide
  - 12-hydroxy-N-(3-(palmitamidomethyl)benzyl)octadecanamide
  - 12-hydroxy-N-(3-(stearamidomethyl)benzyl)octadecanamide
  - N-(3-((12-hydroxyoctadecanamido)methyl)benzyl)icosanamide
  - 18-((3-((12-hydroxyoctadecanamido)methyl)benzyl)amino)-18-oxooctadecan-7-yl 12-hydroxyoctadecanoate
  - N,N'-(1,3-phenylenebis(methylene))distearamide
  - N-(3-(palmitamidomethyl)benzyl)stearamide
  - 18-((3-((12-hydroxyoctadecanamido)methyl)benzyl)amino)-18-oxooctadecan-7-yl stearate
  - 18-oxo-18-((3-(stearamidomethyl)benzyl)amino)octadecan-7-yl stearate
- For the assessment, you provided predictions for the following structures:
  - N,N'-(1,3-phenylenebis(methylene))bis(12-hydroxyoctadecanamide)
  - N-(3-((12-hydroxyoctadecanamido)methyl)benzyl)icosanamide

172 As you have used only 2 structures for the prediction while the Substance is composed of 13 constituents you have not covered all constituents of the Substance.

173 Therefore, you have not demonstrated that the prediction is adequate for the purpose of classification and labelling and/or risk assessment.

16.2.2.2. Lack of documentation of the prediction (QPRF)

174 ECHA Guidance R.6.1.6.3. states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:

- the relationship between the modelled substance and the defined applicability domain;
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

175 You have not provided information about the prediction.

176 In absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.

177 Therefore, the information requirement is not fulfilled.

16.3. Study design

178 Bioaccumulation in fish: aqueous and dietary exposure (Method EU C.13 / OECD TG 305) is the preferred test to investigate bioaccumulation (Guidance on IRs and CSA, Section R.7.10.3.1.). Exposure via the aqueous route (OECD TG 305-I) must be conducted unless it can be demonstrated that:

- a stable and fully dissolved concentration of the test material in water cannot be maintained within ± 20% of the mean measured value, and/or
- the highest achievable concentration is less than an order of magnitude above the limit of quantification (LoQ) of a sensitive analytical method.

179 This test set-up is preferred as it allows for a direct comparison with the B and vB criteria of Annex XIII of REACH.

180 You may only conduct the study using the dietary exposure route (OECD 305-III) if you justify and document that testing through aquatic exposure is not technically possible as indicated above. You must then estimate the corresponding BCF value from the dietary test data according to Annex 8 of the OECD 305 TG and OECD Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation (ENV/JM/MONO(2017)16).

17. Long-term toxicity on terrestrial invertebrates

181 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 (Annex IX, Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

17.1. Triggering of the information requirement

182 Under Annex IX, Section 9.4., Column 2, for substances that have a high potential to adsorb to soil or that are very persistent, long-term toxicity testing must be considered instead of short-term. Guidance on IRs and CSA, Section R.7.11.5.3. clarifies that a substance is considered to be very persistent in soil if it has a half-life >180 days. In the absence of specific soil data, high persistence is assumed unless the substance is readily

biodegradable. A substance is considered to be highly adsorptive if the log K_{ow} > 5 or it is ionisable.

183 Under section 5.2.1. of your IUCLID dossier, you conclude that the Substance is not readily biodegradable and therefore high persistence is assumed.

184 Moreover, the Substance is considered highly adsorptive based on a log K_{oc} >5.63 (based on OECD TG 121).

185 Therefore, the Substance and its constituents have a high potential to adsorb to soil and the Substance is potentially very persistent and information on long-term toxicity on terrestrial invertebrates must be provided.

17.2. Information provided

186 You have provided no information on short-term or long-term toxicity to invertebrates for the Substance.

187 Instead you have adapted this information requirement by using Column 2 of Annex IX, Section 9. 4. To support the adaptation, you have provided the following information: "*Direct exposure of soil is considered unlikely to occur from the use of the substance. There is some potential for environmental release to water from use of the substance. The physico-chemical properties of the substance indicate that any dissolved substance may partition out of the aquatic environment and have potential to bind to sediment/soil particles and surfaces. Indirect exposure of soil cannot therefore be discounted based on the physico-chemical properties of the substance (log Pow, log Koc). Therefore the substance is considered to have some potential to accumulate in the terrestrial compartment, which could lead to exposure to terrestrial organisms through ingestion of soil particles. However, due to the very limited solubility of the test substance, partitioning of dissolved substance may be limited. The derived PNECsoil is not considered to be fully reliable for a comparison against PEC for the terrestrial compartment to indicate whether a study is required. Due to the limited concentration of substance anticipated to be present in the aquatic environment, indirect exposure of soils through partitioning is not anticipated to be significant, and the concentration of the substance is the soil compartments is anticipated to be at levels where significant toxicity should not occur*".

17.3. Assessment of the information provided

17.3.1. The provided adaptation does not meet the criteria of Annex IX, Section 9.4., Column 2

188 Under Annex IX, Section 9.4., Column 2, the study does not need to be conducted if direct and indirect exposure of the soil compartment is unlikely.

189 For the reasons already described in section 13.3.1., you have not demonstrated that exposure to soil is unlikely.

190 Therefore your adaptation is rejected and the information requirement is not fulfilled.

17.4. Study design and test specifications

191 To fulfil the information requirement, the test method(s) according to OECD TG 222, OECD TG 220, and OECD TG 232 are appropriate to cover the information requirement for long-term toxicity on terrestrial invertebrates (Guidance on IRs and CSA, Section R.7.11.3.1). You can choose any of these methods, but you must ensure that the Substance is within the applicability domain of the chosen test method.

18. Effects on soil micro-organisms

192 Effects on soil microorganisms is an information requirement under Annex IX, Section 9.4.2.

18.1. Information provided

193 You have adapted this information requirement by using Column 2 of Annex IX, Section 9. 4. To support the adaptation, you have provided the same justification as already described in Section 17.2.

18.1. Assessment of the information provided

18.1.1. The provided adaptation does not meet the criteria of Annex IX, Section 9.4., Column 2

194 Under Annex IX, Section 9.4., Column 2, the study does not need to be conducted if direct and indirect exposure of the soil compartment is unlikely.

195 For the reasons already described in section 13.3.1., you have not demonstrated that exposure to soil is unlikely.

196 Therefore your adaptation is rejected and the information requirement is not fulfilled.

18.2. Study design and test specifications

197 To fulfil the information requirement for the Substance the Soil Microorganisms: Nitrogen Transformation Test (EU C.21/OECD TG 216) is most appropriate for assessing effects on soil microorganisms for most non-agrochemicals (Guidance on IRs and CSA, Section R.7.11.3.1.).

19. Long-term toxicity on terrestrial plants

198 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 (Annex IX, Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

19.1. Triggering of the information requirement

199 As explained in the request 17.1, the Substance has a high potential to adsorb to soil and is potentially very persistent. On this basis information on long-term toxicity on plants must be provided.

19.1. Information provided

200 You have provided no information on short-term or long-term toxicity to plants for the Substance.

201 Instead you have adapted this information requirement by using Column 2 of Annex IX, Section 9. 4. To support the adaptation, you have provided the same justification as already described in Section 17.2.

19.2. Assessment of the information provided

19.2.1. The provided adaptation does not meet the criteria of Annex IX, Section 9.4., Column 2

202 Under Annex IX, Section 9.4., Column 2, the study does not need to be conducted if direct and indirect exposure of the soil compartment is unlikely.

203 For the reasons already described in section 13.3.1., you have not demonstrated that exposure to soil is unlikely.

204 Therefore your adaptation is rejected and the information requirement is not fulfilled.

19.3. Study design and test specifications

The Terrestrial Plant Test (test method: OECD TG 208, with at least six species)/ ISO 22030 is appropriate to cover the information requirement for long-term toxicity on terrestrial plants. 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.

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).
Guidance for monomers and polymers; ECHA (2023).
***Guidance on intermediates*;** ECHA (2010).
All guidance documents are 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

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 22 February 2023.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 6 months for requests 1 to 3 from the standard deadline granted by ECHA and by 12 months for other requests to take into account currently longer lead times in contract research organisations.

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

ECHA did not receive any comments within the commenting period.

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: Addressee(s) 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]

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 (https://echa.europa.eu/practical-guides).

(4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2 Test material

(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 boundary composition(s) of the Substance,
- the impact of each constituent/group of constituents on the test results for the endpoint to be assessed. For example, if a constituent/group of constituents of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/group of constituents.

(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 the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

With that detailed information, ECHA can confirm 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 (https://echa.europa.eu/manuals).

2. General recommendations for conducting and reporting new tests

2.1. Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituents and, as indicated in Guidance on IRs & CSA, Section R.11.4.2.2, you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach, (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthesize its relevant constituents and/or fractions.

References to Guidance on REACH and other supporting documents can be found in Appendix 1.