~~Confidential~~

Helsinki, 15 March 2023

Addressees
Registrant(s) of DFAS_Di_C18unsat_JS as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
18/02/2022

Registered substance subject to this decision ("the Substance")
Substance name: Oleic acid, compound with (Z)-N-octadec-9-enylpropane-1,3-diamine (2:1)
EC/List number: 251-846-4

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

DECISION ON TESTING PROPOSAL(S)

Under Article 40 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***23 June 2025***.

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

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

1. Long-term toxicity testing on aquatic invertebrates also requested below (triggered by Annex VII, Section 9.1.1., column 2)

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

2. 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

3. 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)

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

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

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
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 decision

Contents

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Reasons for the decision(s) related to the information under Annex VII of REACH

1. Long-term toxicity testing on aquatic invertebrates

1 Short-term toxicity testing on aquatic invertebrates is an information requirement under Column 1 of Annex VII to REACH (Section 9.1.1.). However, long-term toxicity testing on aquatic invertebrates must be considered (Section 9.1.1., Column 2) if the substance is poorly water soluble.

2 Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests do not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (Guidance on IRs and CSA, Section R.7.8.5).

3 Under Section 4.8 of your technical dossier, you have provided a water solubility study similar to OECD TG 123. The saturation concentration of the Substance in water was determined to be c.a. 0.005 mg/L.

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

5 The examination of the information provided as well as the selection of the requested test and the test design are addressed under Request 4.

Reasons for the decision(s) related to the information under Annex VIII of REACH

2. Long-term toxicity testing on fish

6 Short-term toxicity testing on fish is an information requirement under Column 1 of Annex VIII to REACH (Section 9.1.3.). However, long-term toxicity testing on fish must be considered (Section 9.1.3., Column 2) if the substance is poorly water soluble.

7 Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests do not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (Guidance on IRs and CSA, Section R.7.8.5).

8 As already explained under Request 1, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

9 The examination of the information provided, your considerations of alternative methods, of third party comments (if applicable), as well as the selection of the requested test and the test design are addressed under Request 5.

Reasons for the decision(s) related to the information under Annex IX of REACH

3. Pre-natal developmental toxicity study

10 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.).

3.1. Information provided to fulfil the information requirement

11 You have submitted a testing proposal for a PNDT study according to the OECD TG 414 by the oral route with the Substance.

12 ECHA requested your considerations for alternative methods to fulfil the information requirement for Developmental toxicity. You provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

13 ECHA agrees that a PNDT study in a first species is necessary.

3.2. Specification of the study design

14 You proposed testing in the rat as a first species. You may select between the rat or the rabbit because both are preferred species under the OECD TG 414 (ECHA Guidance R.7a, Section R.7.6.2.3.2.).

15 You proposed testing by the oral route. ECHA agrees with your proposal because this route of administration is the most appropriate to investigate reproductive toxicity (ECHA Guidance R.7a, Section R.7.6.2.3.2.).

16 In your comments on the draft decision, you agree to conduct the requested test.

3.3. Outcome

17 Your testing proposal is accepted under Article 40(3)(a), and you are requested to conduct the test, as specified above.

4. Long-term toxicity testing on aquatic invertebrates

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

4.1. Information provided to fulfil the information requirement

19 You have submitted a testing proposal for a Daphnia magna reproduction test (test method: EU C.20/OECD TG 211) with the following justification: "*A Testing Proposal for a long-term toxicity testing on daphnia is submitted in order to perform the study (according to TG OECD 211) with a standard OECD medium*".

20 You have also provided:

(i) a long-term toxicity study on aquatic invertebrates (2012) on the Substance.

21 We have assessed the existing information on long-term toxicity on aquatic invertebrates and we identified the following issue:

4.1.1. The provided long-term study (i) is not reliable.

22 To fulfil the information requirement for long-term toxicity on aquatic invertebrates, 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). The Substance is difficult to test due to the low water solubility (c.a. 0.005 mg/L), adsorptive properties (log Kp > 4) and ionisable properties (pKa for the first amine of > 9). Therefore, the following specifications must be met:

23 Additional requirements applicable to difficult to test substances

Preliminary solubility study

a) if the test material is poorly water soluble, the maximum dissolved concentration that can be achieved in the specific test solution under the test conditions is determined;

b) if the test material is forming dispersion or emulsions (*e.g.* certain surfactants, aliphatic amines), the dispersibility limit or the critical micelle concentration of the test material in the specific test solution under the test conditions is determined;

Test solutions preparation methods

c) 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;

d) demonstration that the stock solution preparation method is of adequate quality (*e.g.* water solubility limit is reached when targeted);

Test design

e) a continuous flow through exposure system is used if exposure concentrations cannot be maintained within 80-120% of nominal in a semi-static exposure system with a renewal frequency of 24 hours.

24 In study (i) described as a long-term toxicity study on daphnids according to OECD TG 211:

25 Additional requirements applicable to difficult to test substances

Preliminary solubility study

a) the Substance is poorly water soluble (*c.a.* 0.005 mg/L based on a study similar to OECD TG 123). However, you have not provided information on the maximum dissolved concentration that can be achieved in the specific test solution under the test conditions;

b) based on structure, the Substance is an aliphatic amine and is therefore likely to form dispersion or emulsions. However, the dispersibility limit or the critical micelle concentration of the test material in the specific test solution under the test conditions is not provided;

Test solutions preparation methods

c) the Substance has a log Kp > 4 and is therefore considered to be adsorptive. However, natural river water of the river Innerste was used as test medium, and you report that the TOC concentration was 3.66 mg/L;

d) you have provided no supporting information to demonstrate that the stock solution preparation method was of adequate quality to reach the water solubility limit;

Test design

e) the test was conducted under semi-static conditions with a renewal rate of 3 times per week. Exposure concentrations was not maintained within 80-120% in old media at 0.5 and 1 mg/L in old media.

26 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically

- the TOC content of the test medium was above the mandatory value of 2 mg/L which may have reduced exposure to the Substance and is therefore not adequate to investigate the intrinsic hazards of the Substance. ECHA notes that information on intrinsic properties of a substance must be generated independently from exposure considerations (*e.g.*, decision of the Board of Appeal of 11 December 2018 in case A-006-2017, para. 133-135). The Guidance on Application of CLP Criteria, Section 1.1.3., specifies 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. Therefore, the bulk approach which aims at mimicking exposure under "more environmentally realistic" conditions must not be used for classification and labelling. 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 under 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.
- as you have not provided information on (i) the saturation limit and critical micelle concentration that can be achieved in the specific test solution under the test conditions and (ii) a demonstration that the test solution was of adequate quality, you have not demonstrated that exposure was adequate during the test;
- the test design for the study was not adequate to maximize the exposure to the test material. The reported results on the analytical monitoring of exposure shows that concentrations were not maintained below ± 20 % of the nominal concentration. However, you have not attempted to increase the frequency of test medium renewal to 24 hours or used a flow-through test set-up as required by the OECD GD 23.

27 Therefore, the study provided in your dossier does not meet the requirements of the OECD TG 211 in conjunction of the OECD GD 23.

28 Therefore, study (i) does not meet the information requirement and ECHA agrees that an appropriate study on long-term toxicity on aquatic invertebrates is needed.

4.1. Test selection and study specifications

29 The proposed Daphnia magna reproduction test (test method: EU C.20/OECD TG 211) is appropriate to cover the information requirement for long-term toxicity on aquatic invertebrates (Guidance on IRs and CSA, Section R.7.8.4.1.).

30 OECD TG 211 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 211. 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 solutions.

31 In your comments on the draft decision, you agree to conduct the requested test.

4.2. Outcome

32 Your testing proposal is accepted under Article 40(3)(a), and you are requested to conduct the test with the Substance, as specified above.

5. Long-term toxicity testing on fish

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

5.1. Information provided to fulfil the information requirement

34 You have submitted a testing proposal for a Fish, Early-Life Stage Toxicity Test (test method: OECD TG 210).

35 Your registration dossier does not include any information on long-term toxicity on fish.

36 ECHA requested your considerations for alternative methods to fulfil the information requirement for long-term toxicity on fish. You provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

37 ECHA agrees that an appropriate study on long-term toxicity on fish is needed.

5.2. Test selection and study specifications

38 The proposed Fish, Early-Life Stage Toxicity Test (test method: OECD TG 210) is appropriate to cover the information requirement for long-term toxicity on fish (Guidance on IRs and CSA, Section R.7.8.4.1.).

39 OECD TG 210 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained under Request 4, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Request 4.

40 In your comments on the draft decision, you agree to conduct the requested test.

5.1. Outcome

41 Your testing proposal is accepted under Article 40(3)(a), and you are requested to conduct the test with the Substance, as specified above.

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 (2012).
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

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 7 March 2022.

ECHA held a third party consultation for the testing proposal(s) from 10 May 2022 until 27 June 2022. ECHA did not receive information from third parties.

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

The deadline of the decision is set based on standard practices for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA 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.

In your comments you agreed to the draft decision. ECHA took your comments into account and did not amend the requests.

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]

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.

(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 (i.e., carbon chain length distribution, unsaturation).

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].

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