~~Confidential~~

Helsinki, 8 December 2022

Addressees
Registrant(s) of JS_26401-35-4 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
16 April 2021

Registered substance subject to this decision ("the Substance")
Substance name: Diisotridecyl adipate
EC number: 247-660-8

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)

Based on Article 40 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***17 March 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 IX of REACH

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

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 request is listed under different Annexes. This is because some information requirements may be triggered already for registrations at lower tonnage band(s). In such cases, only the reasons why the information requirement is triggered are provided in the reasons for the requests from registrants at the lower tonnage band(s). The reasons for the request(s) from registrants at the highest tonnage band concerned then include the reasons why the information requirement is not met and on the specification of the study design. 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

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 an OECD TG 105 study (column elution method). The saturation concentration of the Substance in water was determined to be 0.7 µg/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 Appendix 1, Section 2.

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

2. Long-term toxicity testing on aquatic invertebrates

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

2.1 Information provided to fulfil the information requirement

7 You have submitted a testing proposal for a Daphnia magna reproduction test (test method: EU C.20/OECD TG 211).

8 Your dossier also contains a long-term toxicity study on aquatic invertebrates according to OECD TG 211 with the registered substance.

9 In the justification for the testing proposal, you explain that in the existing study the column elution (CE) method was used for test medium preparation. You specify that this study was requested as part of the Substance evaluation (SEv) process conducted on the Substance in 2016. You raise uncertainties regarding the adequacy of the exposure set-up in this study to reflect truly dissolved concentrations (which varied about two orders of magnitude) and you explain that there was not enough time for an extensive method development project prior to the test was carried out. Therefore, you judge the existing OECD TG 211 study unreliable and thus invalid.

10 Since the 2016 study, you have commissioned two research projects: Fraunhofer project (flow-through silicon tube filing approach) and GAIAC project (semi-static loading by swelling approach) to develop and verify a test procedure and an analytical method, which you consider would enable aquatic toxicity testing of the Substance at its limit of solubility. You indicate that these methods are successful in generating reproducible concentration of the Substance in water. Therefore, you would like to conduct a new long-term toxicity study (OECD TG 211) on aquatic invertebrates using a newly developed passive dosing approach with loading by swelling silicon O-rings in accordance with OECD guidance 23 and Stibany et al. (2017 & 2020). You also note that you will validate the method to determine the test item in aqueous phase according to the requirements of OECD guidance document SANCO3029/99 rev.4.

11 Based on the information provided in the justification for the testing proposal, and the additional information submitted in your comments on the draft decision, ECHA agrees that a new study on long-term toxicity on aquatic invertebrates can be carried out. The generation of new data will add to the pool information on the toxicity of the Substance on aquatic invertebrates.

2.2 Test selection and study specifications

12 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.).

13 The Substance is difficult to test due to its low water solubility (i.e. 0.7 µg/L based on OECD TG 105) and adsorptive properties (log Kow predicted to be 13.03 using US EPA EPI Suite, program KOWWIN v1.67). 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.

14 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 components).

15 The OECD Guideline 23 specifies that a test should be conducted in maximum dissolved concentration that can be achieved in the specific test solution. The maximum achievable dissolved concentration of a test chemical in the test solution, i.e. saturation concentration, may not be the same as the water solubility of the test chemical as determined by, for example, OECD TG 105, as the test solution is much more complex than distilled water. The design of the solubility experiment in test solution should take into account the mixing/contact time to achieve maximum saturation concentration and possible need to remove non-dissolved test chemical from the test solution.

16 Passive dosing matrix preparation

17 In pre-test 1 from the GAIAC report, a justification for the selection of the passive dosing matrix is provided. However, the report does not give adequate justification for method to equilibrate the selected matrix. In pre-test 2 (contrary to pre-test 3 and 4), the matrix was not washed with deionised water prior to the analytical measurement. The available information indicates that washing the matrix might impact the exposure concentration by lowering it. The necessity of this step is not sufficiently elaborated and justified in the report (e.g., by some experimental proof that removing this step would lead to the presence of undissolved material in the test medium).

18 In your comments to the draft decision, you explain the pre-testing you have carried out to justify the selection of a passive dosing material (O-ring) that provides a loading capacity of 1000 x above the expected water solubility and indicates that the 22-hour loading time leads to saturation in the selected material. You also indicate that in this passive dosing method the matrix is loaded in the liquid test substance. You provide experimental data to demonstrate that undissolved residues deposited on the O-ring surface needs non-invasive cleaning referring to the Gaiac Report: Influence of cleansing procedures to the loading of DITA to silicone O-rings that demonstrates that cleaning does not result in a significant loss of the substance. You also note that cleansing of the passive dosing matrix is recommended in Annex 6 of the OECD 23.

19 You summarise that based on your pre-tests a loading time of 48 h is sufficient and after the loading and subsequent cleansing of the matrix, a stable saturation concentration of DITA is maintained over a time-period of 120 h. Considering a medium exchange at least three times a week, you conclude that the sufficient buffer capacity of silicone-rings at the saturation will be provided in the study.

20 ECHA advises you to clearly report the information on the preparation of the passive dosing matrix in the Robust Study Summary.

21 Test medium selection

22 The OECD TG 211 and Guideline 23 recommend that a fully defined medium is used. Elandt M4 and M7 are to date the only fully defined test medium found to be suitable. If you intend to use any other medium, you must demonstrate that it permits to meet the validity criteria of the test guideline (in particular, the mean number of living offspring produced per parent animal surviving at the end of the test must be > 60).

23 In your testing proposal, you do not specify the test medium you are planning to use in the study. You have attached two project reports that explain the pre-testing carried out to prepare for the long-term Daphnia study. In the GAIAC project, you used the standard test medium (Elandt M4), a test medium developed by Fraunhofer and the ADaM medium for conducted preliminary solubility experiments. The report also includes the results of a preliminary long-term Daphnia test conducted using the ADaM medium. In this preliminary experiment, the reproductive output in the control was below the value given as validity criteria in the OECD TG 211. Therefore, it is currently not demonstrated that the ADaM method is appropriate to conduct the requested study.

24 In your comments to the draft decision, you indicate that you intend to use ADaM medium in the study. You explain that it is a fully defined standardized artificial freshwater medium (based on synthetic sea salt and analytical grade chemicals added to deionised water) as required by the OECD TG 211, and it has been used since the beginning of the 90s.

25 You also provide additional experimental data in a form of a report of the Comparative study of DITA in different media in a simplified chronic Daphnia test, Gaiac 2021 to demonstrate that Daphnia produce comparable number of offspring in ADaM and Elandt M4 and above the OECD TG 211 validity criteria. Your further explain that the reduced number of offspring per parent animal in the control of the preliminary long-term Daphnia test conducted with ADaM was caused by an inadequate artificial water used in the test and for the breading stock. This was discovered after the testing during an intensive troubleshooting. For these reasons you expect with high certainty that the ADaM medium permits to meet the validity criteria of the OECD 211 TG.

26 You are allowed to use the ADaM medium in the study requested in this decision. However, you must justify the selection of the medium and you must demonstrate that the validity criteria of the OECD TG 211 have been met in the requested study conducted with this test medium

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

- use loading rates that are sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (Guidance on IRs and CSA, Appendix R.7.8.1-1, Table R.7.8-3);
- 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.

2.3 Outcome

28 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).

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

Read-across assessment framework (RAAF)

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

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

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

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

Appendix 2: Procedure

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 12 July 2021.

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

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

ECHA took into account your comments and amended the requests and the deadline.

Based on your comments and on the available QSAR information for the long-term fish endpoint, ECHA amended the draft decision by removing the requirement to carry out an OECD TG 210 study.

The deadline of the decision was set based on standard practice 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.

Therefore, ECHA has extended the deadline to 24 months.

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

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

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

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

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

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

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.

In your comments to the draft decision you indicate the use of C13 alcohol as test material, to allow direct comparison to the existing OECD TG 211 study. This substance was used during the pre-trials for the chronic *Daphnia* study and for the development of analytical methods to quantify the substance in the test medium in ppb concentrations. Furthermore,

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

you indicate that a similar substance was used for the existing chronic *Daphnia* study carried out as a follow up to the substance evaluation in 2016.

ECHA advises you to clearly report the information on the test material in the Robust Study Summary of the study. You are also reminded of the need for representativeness of the test material for your registration. Technical instructions on how to report the test material information is available in the manual on "How to prepare registration and PPORD dossiers"[3] (Chapter 7).

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.

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