~~Confidential~~

Helsinki, 8 June 2023

Addressees
Registrant as listed in Appendix 3 of this decision.

Date of submission of the dossier subject to this decision
1 March 2022

Registered substance subject to this decision ("the Substance")
Substance name: Reaction products of adipic acid and 2,3-epoxypropyl C10 (branched) alkanoate
EC/List number: 825-846-5

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 ***16 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 (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 (triggered by Annex VIII, Section 9.1.3., column 2).

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 addressee(s) of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

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. In addition, the studies relating to biodegradation and bioaccumulation are necessary for the PBT assessment. However, to determine the testing needed to reach the conclusion on the persistency and bioaccumulation of the Substance you should consider the sequence in which these tests are performed and other conditions described in this Appendix.

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

0. Reasons common to several requests

1 In the comments to the draft decision, you have submitted a new proposal for read-across adaptations under Annex XI, Section 1.5 for the following endpoints:

- Annex VII, 9.1.1., column 2. Long-term toxicity testing on aquatic invertebrates;
- Annex VIII, 9.1.3., column 2. Long-term toxicity testing on fish.

0.1 Assessment of the read-across approach

2 In the comments to the draft decision, you do not agree to perform new studies. Instead, you indicate that you intend to adapt these information requirements by means of grouping and read-across according to Annex XI, Section 1.5, of the REACH Regulation.

3 You refer to three major constituents of the UVCB test substance which all together results in a concentration of [redacted]% of the UVCB substance. You indicate that the three main constituents are [redacted]% similar according to QSAR toolbox similarity profiling and the only dissimilarity being slight differences in carbon number of alkyl group. Therefore, you state that any of the three main constituents could be used as representative constituent of the UVCB. You note that two analogue searches have been carried out for the two major constituents of the UVCB substance and you state that two suitable analogues were found. ECHA hence understands that you propose to predict the long-term toxicity on aquatic invertebrates and long-term toxicity to fish properties of the Substance from studies on these two (analogue) source substances:

- EC No.905-983-8 - Reaction mass of benzyl 2- ethylhexyl adipate and bis(2-ethylhexyl) adipate and dibenzyl adipate mass for the endpoint long-term toxicity on fish;
- EC No. 203-090-1 - Dioctyl adipate for the endpoint long-term toxicity on aquatic invertebrates.

4 You present a hypothesis that source and target substances have similar ecotoxicological properties because they hydrolyse to a common product (isaferat mechanism of action profiling: MechoA 2.1, hydrolysis to narcotic products) and some non-common products (based on slight differences in structure) which are assumed to not assert significant influence on the ecotoxicological profiles. As supporting evidence for the prediction you refer to toxicity data available on ECHA's website and similarities in physicochemical and environmental fate data of the substances. You conclude in your comments that a proper and elaborate justification document for the read-across approach would be provided at later stage if required.

5 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.

6 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).

0.2 Outcome

7 As your strategy relies on a read-across approach that has not yet been fully justified and documented, including bridging studies and other supporting information such as robust study summaries for the source substances, no conclusion on the compliance of the proposed adaptation can be made.

8 Therefore, you remain responsible for complying with the requests 1 and 2 of this decision by the set deadline.

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

1. Long-term toxicity testing on aquatic invertebrates

9 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.

1.1 Triggering of the information requirement

10 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.

11 You have provided information which indicates that the Substance includes constituents that are poorly water soluble. Under Section 4.8 of your technical dossier, you report that only one component of your UVCB substance was analytically determinable. The highest determinable water solubility was 221 µg/L and it was taken as key value.

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

1.2 Information provided to fulfil the information requirement

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

14 Your registration dossier does not include any information on long-term toxicity on aquatic invertebrates.

15 ECHA agrees that an appropriate study on long-term toxicity on aquatic invertebrates is needed.

1.3 Test selection and study specifications

16 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.).

17 The Substance is difficult to test due to the low water solubility (221 µg/L) and adsorptive properties (log K_{ow} between 4.0 and 6.0). 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.

18 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).

19 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.

1.4 Outcome

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

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

2. Long-term toxicity testing on fish

21 Under Article 40(3)(c) of REACH, ECHA may require a registrant to carry out one or more additional tests in case of non-compliance of the testing proposal with requirements set out in Annexes IX and X of the REACH Regulation. You have submitted a testing proposal for the provision of information on aquatic toxicity, which under the provisions of Annexes VII and VIII includes both information on long-term toxicity on invertebrates (Section 9.1.1.) and on fish (Section 9.1.3.) as set out in Annex IX (Sections 9.1.5. and 9.1.6)

- if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

2.1 Triggering of the information requirement

22 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.

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

2.2 Information provided to fulfil the information requirement

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

25 You have adapted this standard information requirement for long-term toxicity to fish by referring to Annex XI, Section 3(a) with the following justification:

i. the Substance's PEC/PNEC ratio is well below 1 (1.66 E-6 mg/L and 1.74 E-7 mg/L for fresh and marine water, respectively) leading to a risk characterisation ratio of ≤ 0.035 given the PNECs for fresh and marine water of 0.05 µg/L and 0.005 µg/L.

ii. despite the fact that the Substance has a high log Kow value (> 3) its bioconcentration factor (BCF) determined by QSAR (using EpiSuite 4.11) is low (97.18-178.4 L/kg wet-wt), which indicates a stronger affinity towards the aqueous environment than the aquatic biomass.

iii. short-term data indicating no need for further investigations is available for all trophic levels and omitting of the fish testing is also in line with the protection and care for animal wellbeing.

Assessment of the information provided

26 A substance-tailored exposure-driven testing adaptation must fulfil the cumulative conditions set out under Annex XI, Sections 3(1) as well as 3(2)(a), (b) or (c).

27 Exposure always well below PNEC not demonstrated

28 Annex XI, Section 3.2.(a)(iii) requires that the results of the exposure assessment must show that exposures are always well below the PNEC, i.e. RCRs must always be well below 1. This means that a high level of confidence is needed to demonstrate that every RCR is low enough to ensure that the risks are always controlled, under every plausible condition of

the manufacture and all identified uses of the Substance. For this purpose, the possible sources of variability and uncertainty must be considered in the assessment of exposure (Guidance on IRs and CSA Chapter R.16, page 68).

29 Uncertainty must be taken into account, either by carrying out the environmental exposure assessment using conservative assumptions and default values, which are provided in Guidance on IRs and CSA Chapters R.16. (Guidance on IRs and CSA Chapter R.19).

30 Alternatively, when the environmental exposure assessment is not based on these generic assumptions, a stepwise, tiered approach including an uncertainty analysis must be conducted. This analysis can be qualitative, deterministic, or probabilistic, to demonstrate that the risk is adequately controlled (Guidance on IRs and CSA Chapter R.19 provides a framework for carrying out a stepwise, tiered approach to uncertainty analysis). The results must be provided in the dossier to demonstrate that the application of such tiered uncertainty analysis gives a clear indication that the risk is adequately controlled (e.g. an increased belief that the (distribution of the) RCR is less than 1).

31 You have provided an exposure assessment reporting 8 exposure scenarios (ES) with qualitative exposure assessment and risk characterisation for each of them.

32 All exposure assessments are not based on the generic assumptions recommended in Guidance on IRs and CSA Chapter R.16, but you have used less conservative input parameters, in particular for the release factors. For example, for ES 6 'widespread use by professional workers leading to inclusion into/onto article (indoor)' you have used release factors to water/air/soil of 0/0/0% instead of the default release factors of 15/5%/'not applicable' recommended in Guidance on IRs and CSA Chapter R.16.

33 You have not provided results of the uncertainty analysis for the environmental exposure assessment ensuring a high level of confidence that the risk is always adequately controlled.

34 Therefore, you have not demonstrated that your exposure assessment is always conservative enough and the RCRs always low enough to cover the possible sources of variability and uncertainty. Thus, exposures cannot be regarded as being always well below the PNEC.

Exposure assessment not provided for all life-cycle stages

35 Under Annex XI, Section 3.2.(a)(i), the exposure assessment must consider all stages of the life-cycle of the Substance resulting from the manufacture and identified uses.

36 In the CSR you provide the following exposure scenarios (ES):

- ES1 Manufacture of the substance,
- ES2 Formulation of the substance,
- ES3-5 Use at industrial sites,
- ES6-7 Widespread use by professional workers, and
- ES8 Service on industrial site.

37 Your CSR does not provide an exposure scenario for

- disposal of stone, plaster, cement, glass and ceramic articles.

38 Therefore, you have not covered all stages of the life-cycle of the Substance.

Low BCF and/or short-term aquatic toxicity data cannot be used to adapt long-term toxicity testing of poorly water soluble substances

39 As far as you justify your adaptation by what is summarized in points (ii) and (iii) above, ECHA points out that Annex XI, Section 3 or other general adaptation rules do not allow adaptation of the requirement for information on long-term toxicity with BCF data and/or data from short-term aquatic studies.

40 As indicated in the reasons for Request 1, 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. Similarly, a low BFC value does not ensure no toxic effects for a poorly soluble substance in long-term aquatic studies.

41 Also, the minimisation of vertebrate animal testing on its own or taken together with the short-term toxicity data and BCF value are no ground for adaptation under the general rules for adaptation.

42 Hence, the information requirement is not fulfilled.

2.3 Test selection and study specifications

43 The 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.).

44 OECD TG 210 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained under request 1, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Test selection and study specifications' under request 1.

2.4 Outcome

45 Therefore, under Article 40(3)(c) of REACH, you are requested to carry out the additional test, 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 2 May 2022.

ECHA held a third-party consultation for the testing proposal(s) from 16 June 2022 until 1 August 2022. ECHA did not receive information from third parties.

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 your tonnage downgrade and amended the requests.

You have provided comments during the decision-making phase indicating a tonnage band downgrade. As a proof of the downgrade you included an extract from your SAP manufacturing data that indicates that the [redacted]. As a result of the registration tonnage band changing from [redacted], the following Annex IX requests were removed from the decision:

- Stability in organic solvents and identity of relevant degradation products,
- Dissociation constant,
- Viscosity,
- Sub-chronic toxicity (90-day), oral route,
- Pre-natal developmental toxicity,
- Soil simulation testing,
- Sediment simulation testing,
- Identification of degradation products.

The deadline of the decision is 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.

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 Annexes VII and VIII to REACH, for registration at 10-100 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[2].

(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 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 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

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

the appropriate analytical methods,
- The reported composition must also include other parameters relevant for the property to be tested, in this case.

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).

This information is needed to assess whether the Test Material is relevant for the Substance.

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

2. General recommendations for conducting and reporting new tests

2.2. 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:

(1) the "known constituents approach" (by assessing specific constituents), or

(2) the "fraction/block approach, (performed on the basis of fractions/blocks of constituents), or

(3) the "whole substance approach", or

(4) 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