~~Confidential~~

Helsinki, 08 June 2023

Addressees
Registrant listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
1 February 2013

Registered substance subject to this decision ("the Substance")
Substance name: Tri-C18-22 (even numbered)-alkyl 2-hydroxypropane-1,2,3-tricarboxylate
EC number: 700-316-5

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***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. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: EU C.4. A/B/C/D/E/F/OECD TG 301A/B/C/D/E/F or EU C.29./OECD TG 310);

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

3. 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

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

5. 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

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

7. 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

0. Reasons common to several requests

0.1. Assessment of the read-across approach

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

- Ready biodegradability (Annex VII, Section 9.2.1.1.);
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.);
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.);
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.).

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

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

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

5 You provide a read-across justification in the endpoint summary of IUCLID Sections 5.2, 6.1 and 7.6 and respective sections of the CSR.

6 You predict the properties of the Substance from information obtained from the following source substance:Tri (hexyl, octyl, decyl) citrate, EC No. EC 430-290-8.

7 You provide the following reasoning for the prediction of environmental fate and ecotoxicological properties: *"The biodegradation of Tri-C18-22 (even numbered)-alkyl 2-hydroxypropane-1,2,3-tricarboxylate was not specifically determined. However, data are available for a structurally related substance Tri (hexyl, octyl, decyl) citrate with the only difference in shorter carbon chain ester groups" and "The acute toxicity of Tri-C18-22 (even numbered)-alkyl 2-hydroxypropane-1,2,3-tricarboxylate towards aquatic species was not specifically determined. However, data for a structurally related substance Tri (hexyl, octyl, decyl) citrate are available with the only difference in shorter carbon chain ester groups. The available data demonstrate a lack of acute toxic effects (NOEC > 100 mg/L) in the range of water solubility, which for the shorter chain esters should even be higher than for the submision substance."*

8 You provide the following reasoning for the prediction of toxicological properties: *"Data are available for a structurally related substance Tri (hexyl, octyl, decyl) citrate with the only difference in the shorter carbon chain length of the ester groups. Due to the structural similarity of the test substance compared to the submission substance the available data can be used for read-across."*

9 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.

10 We have identified the following issue(s) with the prediction(s) of toxicological, ecotoxicological and environmental fate properties:

0.1.1. Missing supporting information to compare the properties of the substances

11 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.).

12 Supporting information must include information to compare properties of the Substance and source substance(s).

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

14 You state that the source substance tri (hexyl, octyl, decyl) citrate and the Substance are structurally related, but you also note the structural difference of the shorter carbon chain length of the ester groups in the source substance. Furthermore, both substances are UVCBs with several isomers and you report the Substance as "*The 3 functional groups (COOH) of citric acid might be esterified with either C18-, C20- or C22-alkyl chain, resulting in numerous isomers and congeners*".

15 In your dossier, for the source substance, you provide the study on *in vitro* chromosome aberration in mammalian cells used in the prediction, as well as a study on *in vitro* gene mutation in bacteria. You provide a study on *in vitro* gene mutation in mammalian cells with the Substance. You have not provided any studies/information with the Substance for the biodegradation screening, effects on algae growth and long-term toxicity to aquatic invertebrates endpoints.

16 *In vitro* studies on gene mutation provide different types of information on genotoxicity compared to the *in vitro* mammalian chromosome aberration study. There is no information on chromosome aberration available for the Substance, therefore the toxicological properties of the Substance and source substance regarding chromosomal aberration cannot be compared. You have not provided any relevant studies or other information to compare the toxicological profile for chromosomal aberration, aquatic toxicity and environmental fate of the Substance and the source substance and to show that the differences in chain length and composition do not influence the toxicological, ecotoxicological and environmental fate properties and that both substances cause the same type of effects.

17 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.

0.1.2. Conclusion on the read-across approach

18 For the reasons above, you have not established that relevant properties of the Substance can be predicted from data on the source substance. Your read-across approaches under Annex XI, Section 1.5. for the information requirements of *in vitro* cytogenicity in

mammalian cells or *in vitro* micronucleus study, biodegradation screening, effects on algae growth and long-term toxicity to aquatic invertebrates are rejected.

0.2. Assessment of your comments on the aquatic toxicity tests requested in the decision

19 In the comments to the draft decision, you disagree to perform the following tests requested to fulfil the standard information requirements:

- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.);
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.);
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

20 In your comments you have not addressed the issues identified in your Annex XI, Section 1.5 adaptation. Instead, you indicate in your comments that testing the aquatic toxicity of the Substance in general may not be technically feasible due to insolubility in water, very poor solubility in organic solvents and the complex UVCB nature of the substance.

21 In your comments to justify the technical difficulties in testing, you first state that the Substance is insoluble in water. You refer to your QSAR model runs in ChemProp v7.0 (UFZ, 2021) as well as US EPA EPI Suite 4.11 (US EPA, 2019), which predict the approximate water solubility of the main component (triester with C18-22 fatty alcohols comprising ca. 95% of the Substance) to be between 10^{-20} mg/L to 10^{-19} mg/L. Water solubility of the minor component of the UVCB, C18-22 fatty alcohols (ca. 5%), is concluded to be higher and you report the value of 1 µg/L for one of the constituents.

22 In your comments you also indicate that you have made attempts to conduct preliminary tests for the *Daphnia magna* short-term toxicity study according to OECD TG 202. You report that your attempts to dissolve the Substance in DMSO using ultrasonication and vortexing were not successful. Also attempts to prepare Water Accomodated Fractions (WAFs) were not successful as the Substance precipitation was observed after 24 hours in the initially clear WAF fraction. Furthermore, the analytical verification of the concentrations via HPLC-MS and GC-MS are not feasible due to poor solubility in solvents and very low volatility.

23 As requested in the decision, you have also considered the approaches described in OECD GD 23 for difficult to test substances. You state in your comments that none of the methods described in the OECD GD 23, i.e. direct addition, generator systems, solvents, and WAFs are appropriate for your substance. On this basis you conclude that aquatic toxicity testing with the tests requested and under the conditions demanded (WAF in the order of magnitude of the water solubility) in the draft decision is technically not feasible and not suitable to generate reliable and sound information as the general preconditions for testing as pointed in OECD GD 23 cannot be met.

24 Moreover, you report in your comments a suggestion for an alternative strategy to conduct the aquatic toxicity testing on your substance. In this alternative strategy, a thin layer of the UVCB substance is created in the bottom of test vessels based on the substance's melting range of 68°C-72°C and non-volatility. Sterile test media are then added and shaken to allow all compounds of the UVCB to reach their saturation concentration in the test medium, followed by the insertion of test organisms into the equilibrated system. However, you report that your initial efforts to test this coating approach with the molten material in glass vessels showed that during freezing at room temperature the substance contracts and breaks, and the fragments detached from glass tend to float in the test medium causing potential interference with the test organisms. You therefore conclude that these first results are discouraging concerning the practical feasibility of this approach.

25 Finally, you conclude that the constituents of the Substance are stable, non-reactive compounds with no indications for any specific biochemical activity and no ecotoxic effects are expected up to their saturation concentration in water.

26 Based on your comments as summarized above, ECHA understands that you intend to adapt the above standard information requirements for aquatic toxicity testing according to Annex XI, Section 2, on the grounds that testing is technically not possible.

27 ECHA agrees that based on the information provided in your comments, the aquatic toxicity testing of your substance appears technically not feasible and your intention to adapt the above information requirements under Annex XI, Section 2 is generally valid.

28 However, you have not provided all relevant documentation for the claims that you make in your comments (e.g. the preliminary tests for OECD TG 202 including the investigations of the methods to preprare the test solutions e.g WAF method). Therefore, independent assessment of the technical feasibility cannot be currently made and the data gaps for the above mentioned information requirements concerning aquatic toxicity remain. You should therefore submit this information in an updated registration dossier by the deadline set in this decision.

Reasons related to the information under Annex VII of REACH

1. Ready biodegradability

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

1.1. Information provided

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

(i) an OECD TG 301B key study on ready biodegradability (1999) with the source substance tri (hexyl, octyl, decyl) citrate, EC 430-290-8;
(ii) an OECD TG 301F supporting study on ready biodegradability (1998) with the source substance tri (hexyl, octyl, decyl) citrate, EC 430-290-8;
(iii) an OECD TG 302C supporting study on inherent biodegradability (2000) with the source substance tri (hexyl, octyl, decyl) citrate, EC 430-290-8.

1.2. Assessment of information provided

31 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

32 Therefore, the information requirement is not fulfilled.

1.3. Study design and test specification

33 The revised introduction to the OECD Guidelines For Testing Of Chemicals, Section 3 Part I states that ready biodegradability tests are intended for pure substances but may also be relevant, on a case-by-case basis, to mixtures of structurally similar chemicals (i.e. which are composed of constituents expected to show similar degradation kinetics). However, such tests are not generally applicable for complex mixtures or substances (i.e. UVCB or multi-constituent substances) containing different types of constituents. For complex substances, a single ready biodegradability test does not allow to conclude on the ready biodegradability of all constituents and therefore, does not fulfil the information requirement.

34 In IUCLID section 1.2, you report a single constituent for the Substance however, you claim that "*The 3 functional groups (COOH) of citric acid might be esterified with either C18-, C20- or C22-alkyl chain, resulting in numerous isomers and congeners, thereby fulfilling the criteria as UVCB*".

35 The Substance is a complex substance, i.e. UVCB.

36 For the reasons provided above, testing on the Substance as a whole does not fulfil the information requirement. For the generation of information on ready biodegradability, you must consider the level of information required for the purposes of classification and labelling and, if applicable to your registration, the PBT/vPvB assessment and the exposure assessment/risk characterisation. In order to conclude on which of constituents of the Substance are and which are not readily biodegradable, you may have to consider conducting more than one study using selected individual constituents and/or fractions. If you choose to test one (or more) fraction(s) of the Substance, you must provide a justification that their constituents within chosen fraction(s) are similar enough so that

similar degradation kinetics can be assumed. If you decide to conduct a single study in order to prove that all constituents of the Substance are readily biodegradable, you must provide a justification that the selected constituent/fraction can be considered a reasonable worst-case for the Substance as a whole in terms of degradation kinetics.

37 Justification for selection of relevant constituent and/or fractions for the testing, must consider degradation kinetics of constituents of the Substance based, as minimum, on the similarity/differences of the chemical structures and the physico-chemical properties of constituents of the Substance. For that purpose, tools and approaches mentioned in Guidance on IRs and CSA, Sections R.7b and R.11 should be considered.

38 In the comments to the draft decision, you state that biodegradability testing using individual fractions of your UVCB substance is not appropriate and rather one biodegradation test with the full UVCB is sufficient and adequate. In your justification for testing the whole UVCB substance, you state that the main component ([redacted]%) of the Substance are mixed esters which are chemically and regarding their physico-chemical properties very similar to each other and thus may be treated as a highly insoluble bloc. Biodegradation testing of pure C18/C20/C22 esters would not represent the actual substance subject to registration and would not lead to representative results for this endpoint.

39 With regard to minor components ([redacted]%) of the UVCB ([redacted]), you state that their potential maximum impact to the total biodegradation extent of the UVCB would be in the range of the inherent experimental variability of the test system.

40 You also inform in your comments that a corresponding test with the full UVCB substance has already been carried out by you and you will include it in a subsequent dossier update.

41 ECHA acknowledges your strategy as regards the testing of the full UVCB substance. However, as no study report on the test alledgly already conducted with the full UVCB substance has been provided with your comments, no assessment or conclusions on the compliance can currently be made. On this basis, the information requirement is currently not fulfilled.

2. Growth inhibition study aquatic plants

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

2.1. Information provided

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

(i) An algae growth inhibition test (1999) with the source substance tri (hexyl, octyl, decyl) citrate, EC 430-290-8.

2.2. Assessment of information provided

44 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

45 In addition, ECHA identified endpoint specific issue addressed below.

2.2.1. Source study not adequate for the information requirement

46 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 201. Therefore, the following specifications must be met:

a) analytical monitoring must be conducted. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided.

47 The study (i) is described as algae growth inhibition test. However, the following specifications are not according to the requirements of OECD TG 201:

a) no analytical monitoring was conducted and no justification was provided of why the analytical monitoring of exposure concentrations is not technically feasible.

48 Based on the above, the study does not provide an adequate and reliable coverage of the key parameter(s) addressed by the OECD TG 201 and this study is not an adequate basis for your read-across predictions.

49 Therefore, the information requirement is not fulfilled.

50 Your comments to the draft decision are addressed in Section 0.2.

2.3. Study design and test specifications

51 The Substance is difficult to test due to the low water solubility (below 1 mg/L based on experimental study and between $9.0e^{-21}$ and $9.5e^{-7}$ mg/L based on QSAR estimation) and adsorptive properties (log kow above 8). 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.

52 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).

53 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.

3. Long-term toxicity testing on aquatic invertebrates (triggered by Annex VII, Section 9.1.1., Column 2)

54 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII, Column 1, 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.

3.1. Triggering of the information requirement

55 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).

56 You have provided information which indicates that the Substance includes constituents that are poorly water soluble. More specifically, you report that the water solubility is ≤ 1 mg/L based on the ASTM E 1148-02 test and between $9.0e^{-21}$ and $9.5e^{-7}$ mg/L based on the QSAR estimation (KOWWIN in the EPISuite v. 4.0).

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

58 The examination of the information provided, as well as the selection of the requested test and the test design are addressed under Request 6.

Reasons related to the information under Annex VIII of REACH

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

59 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

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

(i) an *in vitro* mammalian chromosome aberration test (1999) with the source substance tri (hexyl, octyl, decyl) citrate, EC 430-290-8.

4.2. Assessment of the information provided

61 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

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

4.3. Specification of the study design

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

5. Long-term toxicity testing on fish (triggered by Annex VIII, Section 9.1.3., Column 2)

64 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 must be considered (Section 9.1.3., Column 2) if the substance is poorly water soluble.

5.1. Triggering of the information requirement

65 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).

66 As already explained in Request 3, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

67 The examination of the information provided, as well as the selection of the requested test and the test design are addressed under section 7.

Reasons related to the information under Annex IX of REACH

6. Long-term toxicity testing on aquatic invertebrates

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

6.1. Information provided

69 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 substances:

(i) a study on long-term toxicity to aquatic invertebrates (2004) with the source substance tri (hexyl, octyl, decyl) citrate, EC 430-290-8.

6.2. Assessment of the information provided

70 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

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

72 Your comments to the draft decision are addressed in Section 0.2.

6.3. Study design and test specifications

73 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 and test specifications' under Request 2.

7. Long-term toxicity testing on fish

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

7.1. Information provided

75 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided following information:

(i) "*As Tri-C18-22 (even numbered)-alkyl 2-hydroxypropane-1,2,3-tricarboxylate can not produce aquatic toxicity, it is concluded that in accordance with column 2 of REACH annex IX, the investigation of chronic fish-toxicity is not necessary*."

7.2. Assessment of the information provided

76 We have assessed the information provided and identified the following issue(s):

77 Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1. It must be understood as a trigger for providing further information on long-term toxicity to fish if the chemical safety assessment

according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

78 Your adaptation is therefore rejected and the information requirement is not fulfilled.

79 Your comments to the draft decision are addressed in Section 0.2.

7.3. Study design and test specifications

80 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.).

81 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 and test specifications' under Request 2.

82 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).

83 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.

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

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 27 September 2021.

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

ECHA took into account your comments and did not amend the request(s).

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: 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;

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 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 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,
- 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.

With that detailed information, ECHA can confirm whether the Test Material is relevant for

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

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

2.1. 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