

Helsinki, 11 October 2023

Addressees

Registrants of JS_90193-76-3 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision

02/02/2022

Registered substance subject to this decision ("the Substance")Substance name: 1,2-benzenedicarboxylic acid, di-c16-18-alkyl esters
EC/List number: 290-580-3**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 **19 April 2027**.

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

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

1. Skin sensitisation (Annex VII, Section 8.3.)
 - a) *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (OECD TG 442E) (Annex VII, Section 8.3.1.); and
 - b) only if the *in vitro/in chemico* test methods specified under point a) above are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429);
2. *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, OECD TG 471 (2020))
3. Growth inhibition study on aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3/OECD TG 201)
4. 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

5. *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: EU B.17./OECD TG 476 or EU B.67./OECD TG 490)
6. Justification for an adaptation of the short-term repeated dose toxicity study (28 days) (Annex VIII, Section 8.6.1., Column 2) based on the request 11 below,

or in case the sub-chronic toxicity study (90 days) is not requested:

Short-term repeated dose toxicity study (28 days) (Annex VIII, Section 8.6.1.; test method: EU B.7/OECD TG 407) by oral route, in rats

7. Screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats
8. Sediment simulation testing, also requested below (triggered by Annex VIII, Section 9.2)
9. Identification of degradation products, also requested below (triggered by Annex VIII, Section 9.2)
10. Bioaccumulation in aquatic species, also requested below (triggered by Annex VIII, Section 9.3)

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

11. Sub-chronic toxicity study (90 days), oral route (Annex IX, Section 8.6.2.; test method: OECD TG 408) in rats
12. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)
13. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)
14. Sediment simulation testing (Annex IX, Section 9.2.1.4.; test method: EU C.24/OECD TG 308) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided
15. Identification of degradation products (Annex IX, Section 9.2.3.; test method: EU C.23/OECD TG 308)
16. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method: EU C.13/OECD TG 305)

The reasons for the requests are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The 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. 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.

Authorised¹ under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the requests

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.

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Reasons common to several requests

0.1. Test material not representative of the Substance

- 1 To comply with the information requirement, the test material in a study must be representative for the Substance; Article 10 and Recital 19 of REACH; Guidance on IRs and CSA, Section R.4.1.). The Test Methods Regulation (EU) 440/2008, as amended by Regulation (EU) 2016/266, requires that *"if the test method is used for the testing of a [...] UVCB [...] sufficient information on its composition should be made available, as far as possible, e.g. by the chemical identity of its constituents, their quantitative occurrence, and relevant properties of the constituents"*. Such information includes on the distribution of alkyl chain length and information on the branching of alkyl side carbon chain (i.e., isomeric composition) depending on the type of UVCB substance.
- 2 In requests 1, 3 and 5, the studies have been conducted with the Substance without further information on the distribution of alkyl chain length and information on the branching of alkyl side carbon chain (i.e., isomeric composition).
- 3 In the absence of detailed information on the UVCB test material, such as the distribution of alkyl chain length and information on the branching of alkyl side carbon chain (i.e., isomeric composition), the identity of the test material cannot be assessed. Therefore you have not demonstrated that the test material is representative for the Substance.

0.2. Read-across adaptation rejected

- 4 You have adapted the following standard information requirements by using grouping and read-across approach under Annex XI, Section 1.5.:
- *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.)
 - Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
 - Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
 - Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
 - Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2 and Annex IX, Section 9.1.5)
- 5 ECHA has considered the scientific and regulatory validity of your read-across approach in general before assessing the specific standard information requirements in the following sections.
- 6 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.
- 7 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).
- 8 You provide a read-across justification document in IUCLID Section 13.

0.2.1. Scope of the grouping of substances – identification of source substances

- 9 You predict the properties of the Substance from information obtained from the following source substances:
- 1,2-Benzenedicarboxylic acid, mixed cetyl and stearyl esters, EC 270-487-4 (source substance 1);

- 1,2-Benzenedicarboxylic acid di-C9-11-branched and linear alkyl esters, EC 271-085-1 (source substance 2);
- Ditridecyl phthalate, EC 204-294-3 (source substance 3).

10 You provide the following reasoning for the prediction of (eco)toxicological properties:

- common functional groups;
- common precursors and the likelihood of common breakdown products via biological process/ similar metabolic pathways;
- structural similarity;
- similar physico-chemical properties;
- common properties for environmental fate and eco-toxicological profile;
- common levels and mode of human health related effects.

11 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.

12 We have identified the following issues with the predictions of (eco)toxicological properties:

0.2.1.1. Incomplete characterisation of target and source substances

13 Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as group*".

14 Therefore, qualitative and quantitative information on the compositions of the Substance and of the source substances must be provided, to the extent that this is measurable, to allow assessing whether the attempted predictions are compromised by the composition and/or impurities (Guidance on IRs and CSA, Section R.6.2.5.5.).

15 In addition, the Test Methods Regulation (EU) 440/2008, as amended by Regulation (EU) 2016/266, requires that "*if the test method is used for the testing of a MCS, UVCB or mixture, sufficient information on its composition should be made available, as far as possible, e.g. by the chemical identity of its constituents, their quantitative occurrence, and relevant properties of the constituents*". Such information includes the distribution of alkyl chain length and information on the branching of alkyl side carbon chain (i.e., isomeric composition) depending on the type of UVCB substance.

16 In your read-across justification document, you provide the following information on the target and source substances:

- Target substance (i.e., the Substance): you specify that the fatty alcohol used to manufacture the Substance has the following C-chain length distribution: "< C16: █%; C16: █%, C18: █%; > C18: < █%". You also specify that the residual alcohol content is below 15%.
- Source substance 1: you specify that the fatty alcohol used to manufacture the Substance has the following C-chain length distribution: "C16: █%; C18: █%". No minor constituents or impurities are reported. Therefore, ECHA understands that this substance only includes two constituents.
- Source substance 2: you specify that the fatty alcohol used to manufacture the Substance has the following C-chain length distribution: "C9: █%; C10: █%; C11: █% █% of alcohol linear, predominantly mono-2-methyl branching in the remainder".

- Source substance 3: you only specify the purity of the substance (i.e., >■%). You indicate that this substance includes branched isomers.

17 However, the following information on composition is missing:

- Target: the distribution of C-chain length < C16 and > C18, which can amount up to 11% of the Substance, is not provided.
- Source substance 2: on branching, you state that it corresponds mainly to mono-2-methyl branching. However, you have provided no information on the other branched isomers that may be found in this substance and their relative abundance.
- Source substance 3: the substance includes branched isomers but you provided no information on the nature and quantity of those branched constituents. Also, you specify that the purity of this substance is 80% but you have not defined the remaining 20%.

18 In addition, the studies addressed in requests 2, 7, 11 and 12 have been conducted with the source substance 1 and source substance 2 without further information than the CAS and EC numbers. No information has been provided on purity, composition, carbon chain length, branching, isomeric composition. The study addressed in request 4 and 13 have been conducted with the source substance 3 without further information than the CAS and EC numbers and purity (99.6%).

19 Without adequate qualitative and quantitative information on the compositions of the Substance and of the source substances, it is not possible to assess whether the attempted predictions are compromised by the composition of the source substances.

20 In addition, in the absence of composition information on the test material, the identity of the test material and its impurities cannot be assessed, and you have not demonstrated that the test material is representative for the source substance.

0.2.1.2. Missing supporting information to compare properties of the substances(s)

21 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.).

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

23 For the source substances, you provide the studies used in the prediction in the registration dossier. Apart from studies on the source substances, your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data for the Substance that would confirm that both substances cause the same type of effects. Also, you have provided no supporting information to support that variation in carbon chain length as well as the branching of the alkyl chain would not impact the prediction.

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

0.2.1.3. Inadequate or unreliable studies on the source substances

- 25 According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

- (1) be adequate for the purpose of classification and labelling and/or risk assessment;
- (2) have adequate and reliable coverage of the key parameters addressed in the corresponding study that shall normally be performed for a particular information requirement.

- 26 Specific reasons why the studies on the source substances do not meet these criteria are explained further below under the requests 2, 6, 7, 11, 12, and 13. Therefore, no reliable predictions can be made for these information requirements.

0.2.2. Conclusion on the read-across approach

- 27 For the reasons above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approach under Annex XI, Section 1.5. is rejected.

Reasons related to the information under Annex VII of REACH**1. Skin sensitisation**

28 Skin sensitisation is an information requirement under Annex VII, Section 8.3. Under Section 8.3., Column 1, the registrants must submit information allowing (1) a conclusion whether the substance is a skin sensitizer and (2) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

1.1. Information provided

29 You have provided

(i) a Buehler test (1992) with the Substance.

*1.2. Assessment of the information provided**1.2.1. Assessment whether the Substance causes skin sensitisation**1.2.1.1. Test material in study (i) not representative of the Substance*

30 As explained in Section 0.1., the test material in study (i) is not representative of the Substance. In addition, ECHA identified the endpoint-specific issue addressed below.

1.2.1.2. The provided study does not meet the specifications of the test guideline(s)

31 To fulfil the information requirement, and to enable concluding whether the Substance causes skin sensitisation, a study must comply with the EU Method B.6/OECD TG 406 (Article 13(3) of REACH). Therefore, the following specifications must be met:

- a) the appropriate number of animals is included in the study: 20 in test and 10 in control group;
- b) a positive control is included to establish the sensitivity and reliability of the experimental technique.

32 In study (i):

- a) only 10 animals were used;
- b) no information on a positive control group was provided.

33 The information provided does not cover the specifications required by the EU Method B.6/OECD TG 406.

34 On this basis, it cannot be concluded whether the Substance causes skin sensitisation.

1.2.2. No assessment of potency

35 To be considered compliant and enable a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

36 As the currently available data does not allow to conclude whether the Substance causes skin sensitisation (see section 1.2.1. above), this condition cannot be assessed.

37 Therefore, the information requirement is not fulfilled.

1.3. *Specification of the study design*

38 To fulfil the information requirement for the Substance, information on molecular interaction with skin proteins and inflammatory response in keratinocytes and activation of dendritic cells (OECD TG 442C and OECD TG 442D and OECD TG 442E) must be provided. Furthermore an appropriate risk assessment is required if a classification of the Substance as a skin sensitiser (Cat 1A or 1B) is warranted.

39 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing data or newly generated data, in vivo skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

2. *In vitro* gene mutation study in bacteria

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

2.1. *Information provided*

41 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) an *in vitro* gene mutation study in bacteria (1981) with the source substance 1,2-Benzenedicarboxylic acid, mixed cetyl and stearyl esters, EC 270-487-4.

2.2. *Assessment of the information provided*

2.2.1. *Read-across adaptation rejected*

42 As explained in Section 0.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint specific issue(s) addressed below.

2.2.1.1. *Inadequate or unreliable study on the source substance(s)*

43 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 471. Therefore, the following specifications must be met:

- a) the test is performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101);
- b) the maximum dose tested induces a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose corresponds to 5 mg/plate or 5 µl/plate;

- c) the mean number of revertant colonies per plate is reported for the treated doses and the controls;
- d) negative results are confirmed in a repeat experiment with modification of study parameters to extend the range of conditions assessed, or a justification why confirmation of negative results is not considered necessary is provided.

44 In study (i):

- a) the test was performed with the strains *S. typhimurium* TA 1535, TA 1537, TA 1538, TA 98, TA 100 (i.e., the strain *S. typhimurium* TA102 or *E. coli* WP2 *uvrA* or *E. coli* WP2 *uvrA* (pKM101) is missing);
- b) the maximum dose tested did not induced a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance and it was less than 5 mg/plate or 5 µl/plate;
- c) the mean number of revertant colonies per plate for the treated doses and the controls was not reported;
- d) no repeat experiment was performed to confirm the negative results and no justification was provided.

45 Based on the above, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameter(s) required by the OECD TG 471.

46 Therefore, the information requirement is not fulfilled.

2.3. *Specification of the study design*

47 To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471) is considered suitable.

3. Growth inhibition study aquatic plants

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

3.1. *Information provided*

49 You have provided:

- (i) a growth inhibition study on aquatic plants/algae (2010) with the Substance.

3.2. *Assessment of the information provided*

3.2.1. *Test material in study (i) not representative of the Substance*

50 As explained in Section 0.1., the test material in study (i) is not representative of the Substance. In addition, ECHA identified the endpoint-specific issue addressed below.

3.2.2. *The provided study does not meet the specifications of the test guideline(s)*

51 To fulfil the information requirement, a study must comply with OECD TG 201 and the specifications of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). The Substance is difficult to test as it has low water solubility ($WS < 0.05 \text{ mg/l}$) and high adsorptive properties ($\log K_{ow} > 10$ and $\log K_{oc} > 5$). Therefore, the following specifications must be met:

52 Reporting of the methodology and results

- a) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;
- b) adequate information on the analytical method (including performance parameters of the method) is provided;
- c) as explained above the Substance is difficult to test. Therefore, the following additional information must be provided:
 - o the results of a preliminary solubility and stability study,
 - o a description of the methods used to prepare stock and test solutions,
 - o if the test material is tested at the saturation concentration, evidence that all reasonable efforts have been taken to achieve a saturation concentration,

53 In study (i):

Reporting of the methodology and results

- a) tabulated data on the algal biomass determined daily for each treatment group and control are not reported;
- b) on the analytical method adequate information, you have only reported the analytical limit of detection (LOD of 0.01 mg/L). No other performance parameters of the method are reported, and the measured concentrations were reported to be below the LOD.
- c) the Substance is difficult to test, and you have not provided the information listed above.

54 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, as you have not provided the information listed under point a) to c), ECHA is not in a position to assess whether the validity criteria of the test guideline were met, whether the test conducted under conditions that are consistent with the requirement of the OECD TG 201 and OECD GD 23, and to assess the interpretation of the study results.

55 Therefore, the requirements of OECD TG 201 in combination with OECD GD 23 are not met.

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

57 In your comment to the draft decision, you agreed to perform the requested study.

3.3. Study design and test specifications

58 The Substance is difficult to test due to the low water solubility ($< 0.05 \text{ mg/L}$) and adsorptive properties ($\log K_{ow} > 10$ and $\log K_{oc} > 5$). 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.

- 59 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).
- 60 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.

4. Long-term toxicity testing on aquatic invertebrates

- 61 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.

4.1. Triggering of the information requirement

- 62 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.
- 63 In the provided EU Method A.6 (2010) and OECD TG 201 (2010), the saturation concentration of the Substance in water was determined to be <0.05 mg/L and below the limit of detection of the analytical method (*i.e.*, 0.01 mg/L), respectively.
- 64 Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates must be provided.

4.2. Information requirement not fulfilled

- 65 The information provided, its assessment and the specifications of the study design are addressed under request 13.

Reasons related to the information under Annex VIII of REACH**5. *In vitro* gene mutation study in mammalian cells**

66 An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII, Section 8.4.3., in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

5.1. *Triggering of the information requirement*

67 Your dossier contains (I) a negative result for *in vitro* cytogenicity study in mammalian cells, and (II) inadequate data for the *in vitro* gene mutation study in bacteria.

68 The *in vitro* gene mutation study in bacteria provided in the dossier is rejected for the reasons provided in request 2.

69 The result of the request 2 will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3. is triggered.

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

5.2. *Information provided*

71 You have provided:

(i) an *in vitro* gene mutation study in mammalian cells (2010) with the Substance.

5.3. *Assessment of the information provided***5.3.1. *Test material in study (i) not representative of the Substance***

72 As explained in Section 0.1., the test material in study (i) is not representative of the Substance. In addition, ECHA identified the endpoint-specific issue addressed below.

5.3.2. *The provided study does not meet the specifications of the test guideline(s)*

73 To fulfil the information requirement, a study must comply with the OECD TG 476 or the OECD TG 490 (Guidance on IRs and CSA, Table.7.7-2) (Article 13(3) of REACH). Therefore, the following specifications must be met:

- a) the maximum concentration tested induces 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration corresponds to 10 mM, 2 mg/mL or 2 µL/mL, whichever is the lowest.

74 In study (i):

- b) the maximum tested concentration did not induce 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance, and it was less than 10 mM, 2 mg/mL or 2 µL/mL.

75 The information provided does not cover the specification(s) required by the OECD TG 476/490.

76 Therefore, the information requirement is not fulfilled.

5.4. Specification of the study design

77 To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xpvt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

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

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

6.1. Information provided

79 ECHA understands that you have adapted this information requirement by using Annex VIII, Section 8.6.1., Column 2. To support the adaptation, you have provided the following information:

- (i) a sub-chronic toxicity study (1971-1972) with the source substance 1,2-Benzenedicarboxylic acid, mixed cetyl and stearyl esters, EC 270-487-4.

6.2. Assessment of the information provided

6.2.1. Study not reliable

80 Under Annex VIII, Section 8.6.1., Column 2, Paragraph 1, Indent 1, the study may be omitted if a reliable sub-chronic (90 days) or chronic toxicity study is available or proposed by the registrant.

81 The study (i) is described as a sub-chronic (90 days) study.

82 However, for the reasons explained in request 11 the study is not reliable.

83 Based on the above, your adaptation is rejected.

84 Therefore, the information requirement is not fulfilled.

6.3. Specification of the study design

85 Following the criteria provided in Annex VIII, Section 8.6.1., Column 2, and considering the Guidance on IRs and CSA, Section R.7.5.6.3.1., the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance.

86 According to the OECD TG 407, the rat is the preferred species.

87 Therefore, the study must be performed according to the OECD TG 407, in rats and with oral administration of the Substance.

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

88 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 11).

- 89 According to Annex VIII, Section 8.6.1., Column 2 and to prevent unnecessary animal testing, a short-term toxicity study (28 days) does not need to be conducted. Therefore, to comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to provide a justification for adaptation, as provided in Annex VIII, Section 8.6.1., Column 2.
- 90 In case the adopted decision no longer contains a request for a 90-day study, you are required to provide a 28-day study.
- 91 Therefore, you are requested to either submit:
- a justification for the adaptation according to Annex VIII, Section 8.6.1., Column 2, based on request 11; or
 - a 28-day study as per the study design described in section 6.3. in case the 90-day study is not requested in the adopted decision.

7. Screening study for reproductive/developmental toxicity

- 92 A screening study for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1., if there is no evidence from analogue substances, QSAR or *in vitro* methods that the substance may be a developmental toxicant.

7.1. Information provided

- 93 ECHA understands that you have adapted this information requirement by using Annex VIII, Section 8.7.1., Column 2. To support the adaptation, you have provided the following information:

- (i) a two-generation reproductive toxicity study (publication, 2000) with the source substance 1,2-Benzenedicarboxylic acid, di-C9-11-branched and linear alkyl esters, EC 271-085-1.

7.2. Assessment of the information provided

7.2.1. The available study is not reliable

- 94 Under Annex VIII, Section 8.7., Column 2, the study does not need to be conducted if a two-generation reproductive toxicity study (OECD TG 416) is available.

- 95 The study (i) is described as a two-generation reproductive toxicity study.

- 96 However, we have identified the following issue(s) with the study:

7.2.1.1. Read-across adaptation rejected

- 97 As explained in Section 0.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint specific issue(s) addressed below.

7.2.1.1.1. Inadequate or unreliable study on the source substance

- 98 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 416. Therefore, the following specifications must be met:

- a) the key parameters for endocrine modes of action are examined;
- b) the key parameters for systemic toxicity are examined.

99 In study (i):

- a) the key parameters for endocrine modes of action were not examined; In particular, anogenital distance, nipple retention, thyroid hormone measurements have not been performed;
- b) the systemic toxicity was not investigated; In particular, the following investigations are missing: full clinical chemistry (P0 and F1), full haematology (P0 and F1) have not been performed.

100 Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameter(s) of the corresponding OECD TG.

101 Based on the above, your adaptation is rejected, and the information requirement is not fulfilled.

7.3. Specification of the study design

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

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

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

8. Sediment simulation testing

105 Under Annex VIII, Section 9.2., Column 2, further information on degradation or further testing as described in Annex IX must be generated if the chemical safety assessment (CSA) in accordance with Annex I indicates the need to investigate further the degradation of the substance.

8.1. Triggering of the information requirement

106 This information requirement is triggered in case, for example, additional information on bioaccumulation as set out in Annex XIII, point 3.2.2., is required to assess PBT or vPvB properties of the substance in accordance with subsection 2.1 of that Annex. This is the case if the Substance itself or any of its constituent or impurity present in concentration \geq 0.1% (w/w) or relevant transformation/degradation product meets the following criteria:

- it is potentially persistent or very persistent (P/vP) as it is not readily biodegradable (*i.e.* $<60/70\%$ degradation in an OECD 301/310), and
- it is potentially bioaccumulative or very bioaccumulative (B/vB) as it has a high potential to partition to lipid storage (*e.g.* $\log K_{ow} > 4.5$)
- it meets the T criteria set in Annex XIII: NOEC or $EC_{10} < 0.01$ mg/L or classification as carc. 1A or 1B, muta. 1A or 1B, repro. 1A, 1B or 2, or STOT RE 1 or 2.

107 Your registration dossier provides the following:

- the Substance is not readily biodegradable (51.1% degradation after 28 days in

- OECD TG 301B (2010);
- the Substance has a high potential to partition to lipid storage ($\log K_{ow} > 10$ based on QSAR predictions).
- it is not possible to conclude on the toxicity of the Substance (see requests 2, 3., 5 to 7, 4. and 11 to 13. of this decision).

108 Based on the above, the available information on the Substance indicates that it is a potential PBT/vPvB substance.

109 Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

110 In your comments to the draft decision, you indicate a testing strategy that rely on conducting an enhanced ready biodegradability study (i.e., an OECD TG 301B study extended to 60 days) in order to assess whether the Substance may be P/vP. You propose to re-evaluate the need to conduct sediment simulation testing under Annex VIII, Section 9.2, column 2 based on the results of the enhanced ready biodegradability study.

111 ECHA takes note of your intention. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline. Your substance contains multiple constituents. Appendix 4, Section 2, of this decision includes recommendations for conducting and reporting environmental tests for substances containing multiple constituents. Since individual constituents contribute differently to degradation, the composition of the test material and the determination of the calculation basis must be documented with particular care.

8.2. Information requirement not fulfilled

112 The information provided, its assessment and the specifications of the study design are addressed under request 14.

9. Identification of degradation products

113 Under Annex VIII, Section 9.2., Column 2, further information on degradation or further testing as described in Annex IX must be generated if the chemical safety assessment (CSA) in accordance with Annex I indicates the need to investigate further the degradation of the substance.

9.1. Triggering of the information requirement

114 This information requirement is triggered in case if for example additional information on degradation as set out in Annex XIII, point 3.2.1, is required to assess PBT or vPvB properties of the substance in accordance with subsection 2.1 of that Annex.

115 As already explained in request 8., the Substance is a potential PBT/vPvB substance.

116 Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

117 In your comments to the draft decision, you indicate a testing strategy that rely on conducting an enhanced ready biodegradability study (i.e., an OECD TG 301B study extended to 60 days) in order to assess whether the Substance may be P/vP. You propose to re-evaluate the need to provide information on identification of degradation products

under Annex VIII, Section 9.2, column 2 based on the results of the enhanced ready biodegradability study.

- 118 ECHA takes note of your intention. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

9.2. Information requirement not fulfilled

- 119 The information provided, its assessment and the specifications of the study design are addressed under request 15.

10. Bioaccumulation in aquatic species

- 120 Under Annex VIII, Section 9.3., Column 2, further information on bioaccumulation or further testing as described in Annex IX must be generated if the chemical safety assessment (CSA) in accordance with Annex I indicates the need to investigate further the bioaccumulation properties of the substance.

10.1. Triggering of the information requirement

- 121 Therefore, this information requirement is triggered in case if for example additional information on bioaccumulation as set out in Annex XIII, point 3.2.2, is required to assess PBT or vPvB properties of the substance in accordance with subsection 2.1 of that Annex.
- 122 As already explained in request 8, the Substance is a potential PBT/vPvB substance.
- 123 Therefore, the chemical safety assessment (CSA) indicates the need for further investigation on bioaccumulation in aquatic species.

10.2. Information requirement not fulfilled

- 124 The information provided, its assessment and the specifications of the study design are addressed under request 16.

Reasons related to the information under Annex IX of REACH**11. Sub-chronic toxicity study (90 days)**

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

11.1. Information provided

126 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 sub-chronic toxicity study (1971-1972) with the source substance 1,2-Benzenedicarboxylic acid, mixed cetyl and stearyl esters, EC 270-487-4.

*11.2. Assessment of the information provided**11.2.1. Read-across adaptation rejected*

127 As explained in Section 0.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

11.2.1.1. Inadequate or unreliable study on the source substance(s)

128 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 408. Therefore, the following specifications must be met:

- a) the oestrus cycle in females is examined at necropsy.

129 However, in study (i):

- a) oestrus cyclicity was not assessed.

130 Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameter of the corresponding OECD TG.

131 Therefore, the information requirement is not fulfilled.

11.3. Specification of the study design

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

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

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

12. Pre-natal developmental toxicity study in one species

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

12.1. Information provided

136 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 pre-natal developmental toxicity study in rats (2001) with the source substance 1,2-Benzenedicarboxylic acid, di-C9-11-branched and linear alkyl esters, EC 271-085-1;
- (ii) a pre-natal developmental toxicity study in rats (1983) with the source substance 1,2-Benzenedicarboxylic acid, mixed cetyl and stearyl esters, EC 270-487-4.

12.2. Assessment of the information provided

12.2.1. Read-across adaptation rejected

137 As explained in Section 0.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

12.2.1.1. Inadequate or unreliable studies on the source substance(s)

138 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 be normally performed for a particular information requirement, in this case OECD TG 414. Therefore, the following specifications must be met:

- a) at least three dose levels are tested (unless conducted at the limit dose) with concurrent controls.

However, in study (ii), only one dose level was included;

- b) the test chemical is administered via oral gavage.

However, in study (ii), the substance was administered in the diet without justification;

- c) the dams are examined for any structural abnormalities, weight and histopathology of the thyroid gland, thyroid hormone measurements, gravid uterus weight, and uterine content.

However, in studies (i) and (ii), data on the examination of the dams, including incidence and severity, are missing. In particular, the following investigations are missing: weight and histopathology of the thyroid gland, thyroid hormone measurements gravid uterine weight (study ii only);

- d) the fetuses are examined for body weight, number and percent of live and dead fetuses and resorptions, sex ratio, external, skeletal and soft tissue alterations (variations and malformations), measurement of anogenital distance in all live rodent fetuses.

However, in study (ii), data on the examination of the fetuses, including

incidence and severity, are missing; In particular, the following investigations are missing: sex ratio of the fetuses.

139 Therefore, the studies submitted in your adaptation, as currently reported in your dossier, do not provide an adequate and reliable coverage of the key parameters of the corresponding OECD TG.

140 Therefore, the information requirement is not fulfilled.

12.3. Specification of the study design

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

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

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

13. Long-term toxicity testing on aquatic invertebrates

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

13.1. Information provided

145 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 long-term toxicity study on *Daphnia magna*, OECD TG 211 (1998) with the source substance ditridecyl phthalate, EC 204-294-3.

13.2. Assessment of the information provided

13.2.1. Read-across adaptation rejected

146 As explained in Section 0.2., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint specific issue(s) addressed below.

13.2.1.1. Inadequate or unreliable study on the source substance

147 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 211, and meet the specifications of OECD GD 23 if the substance is difficult to test. Therefore, the following specifications must be met:

Reporting of the methodology and results

- a) the full record of the daily production of living offspring during the test by each parent animal is provided.
- b) the Substance is difficult to test. Therefore, the following additional information must be provided:

- the results of a preliminary solubility and stability study,
 - a description of the methods used to prepare stock and test solutions,
 - if the test material is tested at the saturation concentration, evidence that all reasonable efforts have been taken to achieve a saturation concentration.
- c) the number of deaths among the parent animals (if any) and the day on which they occurred is reported

148 In study (i):

Reporting of the methodology and results

- a) You have provided only the mean cumulative number of juveniles produced per alive adult, and not for each parent animal.
- b) You have provided none of the information listed above under point b).
- c) you have reported that "*Mortality of parent animals: control: 20%, vehicle control: 10%, 10 mg/L: 10%*". However you did not report the dates on which they occurred.

149 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, as you have not provided the information listed above under points a) to c), ECHA is not in a position to assess whether the test was conducted under conditions that are consistent with the test guideline specifications in combination with the OECD GD 23, whether the validity criteria were met and to assess the interpretation of the study results.

150 Therefore, the study (i) does not provide an adequate and reliable coverage of the key parameter(s) addressed by the OECD TG 211 in combination with OECD GD 23 and the study (i) is not an adequate basis for your read-across predictions.

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

152 In your comment to the draft decision, you agreed to perform the requested study.

13.3. Study design and test specifications

153 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 3.

14. Sediment simulation testing

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

155 The Substance has a low water solubility (<0.05 mg/L), high partition coefficient (log K_{ow} >10) and high adsorption coefficient (log $K_{oc,soil}$ >5) and therefore has high potential for adsorption to sediment.

14.1. Information provided

156 You have provided the following justifications:

- (i) "No studies investigating the biodegradation of the substance in sediment are available."
- (ii) "*The results from the ready biodegradability test (51.5% after 28 days) show that*

a certain degree of biodegradation of this substance in the environment can be expected”.

14.2. Assessment of the information provided

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

- 157 A registrant may only adapt this information requirement based on the general rules set out in Annex XI. It is noted that Column 2 of Annex IX, Section 9.2., does not allow omitting the need to submit information on sediment simulation testing under Column 1.
- 158 Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH.
- 159 Therefore, you have not demonstrated that this information can be omitted and the information requirement is not fulfilled.
- 160 As already explained under request 8, you propose to first conduct an enhanced ready biodegradability study (i.e., an OECD TG 301B study extended to 60 days) in order to assess whether the Substance may be P/vP. You propose to re-evaluate the need to conduct sediment simulation testing based on the results of the enhanced ready biodegradability study.
- 161 ECHA takes note of your intention and points out that an enhanced degradation screening study it is not a standard information requirement for which testing is requested in this decision. In any case, you remain responsible for submitting, by the set deadline, the required information or providing a valid adaptation of this standard information requirement in accordance with the specific rules for adaptation of column 2 of Section 9.2.1.4. of Annex IX or with the general rules for adaptation of Annex XI.

14.3. Study design and test specifications

- 162 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):
- (1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
 - (2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.
- 163 In accordance with the specifications of OECD TG 308, you must perform the test using two sediments. One sediment should have a high organic carbon content (2.5-7.5%) and a fine texture, the other sediment should have a low organic carbon content (0.5-2.5%) and a coarse texture. If the Substance may also reach marine waters, at least one of the water-sediment systems should be of marine origin.
- 164 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 308.
- 165 In accordance with the specifications of OECD TG 308, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents (Guidance on IRs and CSA, Section R.7.9.4.1.). By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section

R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

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

15. Identification of degradation products

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

168 You have not submitted any information for this requirement.

169 Therefore, the information requirement is not fulfilled.

170 As already explained under request 9, you propose to first conduct an enhanced ready biodegradability study (i.e., an OECD TG 301B study extended to 60 days) in order to assess whether the Substance may be P/vP. You propose to re-evaluate the need to provide information on identification of degradation products based on the results of the enhanced ready biodegradability study.

171 ECHA takes note of your intention and points out that an enhanced degradation screening study it is not a standard information requirement for which testing is requested in this decision. In any case, you remain responsible for submitting, by the set deadline, the required information or providing a valid adaptation of this standard information requirement in accordance with the specific rules for adaptation of column 2 of Section 9.2.3. of Annex IX or with the general rules for adaptation of Annex XI.

15.1. Study design and test specifications

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

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

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

174 You must obtain this information from the degradation study requested in request 14.

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

16. Bioaccumulation in aquatic species

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

16.1. Information provided

177 You have qualified the information provided as a weight of evidence adaptation (WoE, Annex XI, Section 1.2.). However, ECHA understands that the purpose of the justification you provided aims at justifying that the condition required under Column 2 of Annex IX, Section 9.3.2. are met. Therefore, ECHA has assessed the provided information on that basis. In support of your adaptation you provided the following information:

- (i) Justification on how the source of information (ii)-(v) below combined are used to cover the data requirement;
- (ii) QSAR prediction on C16 component, predicting low BCF (BCF=0.89 L/kg whole body w.w.), and you state that *"it can be assumed that the bioaccumulation potential of the substance is low"*;
- (iii) QSAR prediction on C18 component, predicting low BCF (BCF=0.89 L/kg whole body w.w.), and you state that *"it can be assumed that the bioaccumulation potential of the substance is low"*;
- (iv) A literature study by [REDACTED] (2007) addressing the effects of molecular size and lipid solubility on the bioaccumulation potential of environmental contaminants;
- (v) A scientific publication by Nendza and Müller (2010) *"Screening for low bioaccumulation (1): Lipinski's 'Rule of 5' and molecular size"*.

178 You have also provided the following justification: *"Due to its log K_{oc} value of > 5, significant adsorption of this substance to activated sludge in conventional STPs will take place and only low concentrations are expected to be released (if at all) into the environment"*. ECHA assumes that you provided this justification in an attempt to adapt the information requirement under Section 9.3.2., Column 2, second indent of Annex IX to REACH.

16.2. Assessment of information provided

16.2.1. The provided adaptation does not meet the criteria of Annex IX, Section 9.3.2., Column 2

16.2.1.1. Low potential to cross biological membranes

179 Under Section 9.3.2., Column 2, first indent, Annex IX to REACH, the study may be omitted if the Substance is unlikely to cross biological membranes. Guidance on IRs and CSA, Section R.7.8.5. explains that there is no scientific basis to define molecular characteristics that would render a substance unlikely to cross biological membranes. In this context, the indicators used for low likelihood of a high bioaccumulation potential (Guidance on IRs and CSA, Section R.11, Figure R.11-4) must be considered, including:

- physico-chemical indicators of hindered uptake due to large molecular size (e.g. $D_{\max} > 17.4 \text{ \AA}$ and $MW > 1100$ or $MML > 4.3 \text{ nm}$) or high octanol-water partition coefficient ($\log K_{ow} > 10$) or low potential for mass storage (octanol solubility (mg/L) $< 0.002 \times MW$), and
- supporting experimental evidence of hindered uptake (no chronic toxicity for mammals and birds, no chronic ecotoxicity, no uptake in mammalian toxicokinetic studies, very low uptake after chronic exposure).

180 Your registration dossier provides:

- physico-chemical indicators which you consider supportive of hindered uptake:
 - large molecular size: 615 to 671 g/mol
 - high octanol-water partition coefficient ($\log K_{ow} > 10$) would result in low BCF as supported by QSAR predictions. However, you also state that “*since the substance is outside the Kow range of the training set, the results should be taken with caution*” and that the Substance is “*outside the applicability domain of the model (i.e. BCFBAF v3.01)*”.
- physico-chemical indicators which you consider supportive of hindered uptake
 - reported molecular weight is below $MW > 1100$.
 - The QSAR predictions for $\log K_{ow}$ are not reliable as the Substance is outside of the applicability domain. Furthermore, the predictions do not cover all relevant constituents of the Substance. As a result, the predicted BCF cannot be used to support low bioaccumulation potential.

181 Available information on the Substance do not support that the Substance is unlikely to cross biological membranes because your justification does not include reliable indications from physico-chemical indicators combined with experimental evidence to support hindered uptake.

182 Therefore, your adaptation is rejected.

16.2.1.1. Lack of direct and indirect exposure of the sediment compartment is not demonstrated

183 Under Section 9.3.2., Column 2, second indent of Annex IX to REACH, the study may be omitted if direct and indirect exposure of the aquatic compartment is unlikely. The results of the exposure assessment covering all relevant exposure throughout the life cycle of the substance must demonstrate absence of or no significant exposure in all scenarios of the manufacture and all identified uses.

184 The CSR attached to your IUCLID dossier does not include an exposure assessment.

185 Therefore, you have not demonstrated that direct and indirect exposure of the sediment compartment is unlikely. Consequently, your adaptation is rejected.

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

187 In your comment to the draft decision, you agreed to perform the requested study.

16.3. Study design and test specifications

188 Bioaccumulation in fish: aqueous and dietary exposure (Method EU C.13 / OECD TG 305) is the preferred test to investigate bioaccumulation (Guidance on IRs and CSA, Section R.7.10.3.1.). Exposure via the aqueous route (OECD TG 305-I) must be conducted whenever technically feasible. The low water solubility (< 0.05 mg/L) and the high adsorption potential ($\log K_{oc} > 5$) of the Substance indicate significant uncertainty on the feasibility of a study using aqueous exposure. Therefore, in this case, the test is requested to be performed using dietary exposure. You must also attempt to estimate the corresponding BCF value from the dietary test (OECD 305-III) data according to Annex 8 of the OECD 305 TG and OECD Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation (ENV/JM/MONO (2017)16).

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

The information requirement for long-term toxicity testing on fish (Annex IX, Section 9.1.6.) is not addressed in this decision. This is because information that will be generated from the studies requested in the present decision is needed:

- to inform on the potential endocrine disrupting properties of the Substance; and
- to decide on the most appropriate test(s) to meet the information requirement.

The above information requirement may be addressed in a separate decision at a later stage.

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 07 December 2021.

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

ECHA took into account your comments and did not amend the requests.

In your comments on the draft decision, you requested an extension of the deadline to provide information from 39 to 57 months from the date of adoption of the decision. You justify the need to extend the deadline by the additional testing you wish to conduct to assess persistency of the Substance (i.e., enhanced ready biodegradation test). You also claim possible delays due to limited capacity in Contract Research Organizations (CRO).

The timeline set in this decision allows for generating the standard information requirements covered by this decision. In case you decide to submit an adaptation instead of the requested study(ies), it remains your responsibility to provide a compliant adaptation by the set deadline. Second, you have not provided any documentary evidence to substantiate your request based on the limited capacity in the CRO.

On this basis, ECHA has not modified the deadline to provide the information. ECHA took into account your comments and did not amend the request(s) and the deadline.

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

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s) and referred the modified draft decision to the Member State Committee.

You did not provide any comments on the proposed amendment(s).

The Member State Committee unanimously agreed on the draft decision in its MSC-83 written procedure. ECHA adopted the decision under Article 51(6) 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, VIII and IX to REACH, for registration at 100-1000 tpa;

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

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. Test methods, GLP requirements and reporting

- (1) Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.
- (2) Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.
- (3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries².
- (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

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

(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 also include other parameters relevant for the property to be tested, in this case the distribution of alkyl chain length and

² <https://echa.europa.eu/practical-guides>

information on the branching of alkyl side carbon chain (i.e., isomeric composition).

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers (<https://echa.europa.eu/manuals>).

2. General recommendations for conducting and reporting new tests

2.1. Strategy for the PBT/vPvB assessment

Under Annex XIII, the information must be based on data obtained under conditions relevant for the PBT/vPvB assessment. You must assess the PBT properties of each relevant constituent of the Substance present in concentrations at or above 0.1% (w/w) and of all relevant transformation/degradation products. Alternatively, you would have to justify why you consider these not relevant for the PBT/vPvB assessment.

You are advised to consult Guidance on IRs & CSA, Sections R.7.9, R.7.10 and R.11 on PBT assessment to determine the sequence of the tests needed to reach the conclusion on PBT/vPvB. The guidance provides advice on 1) integrated testing strategies (ITS) for the P, B and T assessments and 2) the interpretation of results in concluding whether the Substance fulfils the PBT/vPvB criteria of Annex XIII.

In particular, you are advised to first conclude whether the Substance fulfils the Annex XIII criteria for P and vP, and then continue with the assessment for bioaccumulation. When determining the sequence of simulation degradation testing you are advised to consider the intrinsic properties of the Substance, its identified uses and release patterns as these could significantly influence the environmental fate of the Substance. You must revise your PBT assessment when the new information is available.

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:

- 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.