~~Confidential~~

Helsinki, 11 October 2023

Addressees
Registrants of DTDP JS EM Lead (multi) as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
13/07/2015

Registered substance subject to this decision ("the Substance")
Substance name: 1,2-Benzenedicarboxylic acid, di-C11-14-branched alkyl esters, C13-rich
EC number/List number: 271-089-3

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 ***18 January 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. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: OECD TG 471, 2020)

2. Growth inhibition study on 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. Only if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained, *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)

5. 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 6 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

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

6. Sub-chronic toxicity study (90 days), oral route (Annex IX, Section 8.6.2.; test method: OECD TG 408) in rats

7. Pre-natal developmental toxicity study in one species (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

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

9. Long-term toxicity testing on terrestrial invertebrates (triggered by Annex IX, Section 9.4.1., column 2; test method: EU C.33/OECD TG 222 or EU C.32/OECD TG 220)

10. Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: EU C.21./OECD TG 216

11. Long-term toxicity to terrestrial plants (triggered by Annex IX, Section 9.4.3., column 2; test method: EU C.31./OECD TG 208 with at least six species or ISO 22030)

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

12. Pre-natal developmental toxicity study in a second species (Annex X, Section 8.7.2.; test method: OECD TG 414) by oral route, in a second species (rabbit or rat)

13. Long-term toxicity testing on terrestrial invertebrates (Annex X, Section 9.4.4.; test method: EU C.33/OECD TG 222 or EU C.32/OECD TG 220

14. Long-term toxicity on terrestrial plants (Annex X, Section 9.4.6.; test method: EU C.31/OECD TG 208 with at least six species tested or ISO 22030)

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.

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 request(s)
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 request(s)

Contents

Reasons common to several requests

0.1. Test material not representative of the Substance

1 To comply with an 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 The studies submitted for Growth inhibition study on aquatic plants and Long-term toxicity testing on aquatic invertebrates 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.)
- *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Long-term toxicity testing on terrestrial invertebrates (Annex X, Section 9.4.4.)
- Long-term toxicity on terrestrial plants (Annex X, Section 9.4.6.)

5 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.

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).

0.2.1. Scope of the grouping of substances (category)

8 You provide a read-across justification document in your CSR.

9 For the purpose of this decision, the following category members are listed in the read-across justification document:

10 You predict the properties of the Substance from information obtained from the following source substance(s):

- DIUP 1,2-Benzenedicarboxylic acid, di-C10-12-branched alkyl esters, EC 700-989-5 (source substance 1);
- L9-11P 1,2-Benzenedicarboxylic acid di-C9-11-branched and linear alkyl esters, EC 271-085-1/ CAS RN 68515-43-5 (source substance 2);
- DIDP 1,2-Benzenedicarboxylic acid di-C9-11-branched alkyl esters, C10-rich, EC 271-091-4/ CAS RN 68515-49-1 (source substance 3);
- DINP 1,2-Benzenedicarboxylic acid di-C8-10-branched alkyl esters,C9-rich, EC 271-090-9/ CAS NR 68515-48-0 (source substance 4);
- DIDP, 1,2-benzenedicarboxylic acid, di-isodecyl ester, EC 247-977-1, CAS RN 26761-40-0 (source substance 5);
- DUDP, diundecyl phthalate, EC 222-884-9, CAS RN 3648-20-2 (source substance 6);
- DnOP, dioctyl phthalate, EC 204-214-7, CAS RN 117-84-0 (source substance 7).
- ditridecyl phthalate, EC 204-294-3/ CAS RN 119-06-2 (source substance 8).

11 You justify the grouping of the substances as: "*the target and source substance belong to the High Molecular Weight Phthalate Ester (HMWPE) Category which was established based on structural similarity. As described in below, these substances are similar in molecular structure, physicochemical properties, use, and manufacturing processes. Based on these unifying considerations, the variation in carbon backbone length among these analogues is not expected to significantly impact toxicity. When possible data from the source substance(s) with a carbon backbone length closest to target substance was preferred and used to fulfill individual endpoints. Therefore, it is scientifically reasonable to predict the toxicological properties for the registered substance from the properties determined for the analogues*".

12 In the comments to the draft decision, you suggest a different read-across approach for human health endpoints based on a category of three high molecular phthalates (DIDP with EC 271-091-4, DIUP with EC 700-989-5 and DTDP with EC 271-089-3). We understand from your comments that you propose a "*phase approach to testing*" to decide between performing the studies (skin sensitisation, mutagenicity, reproductive and developmental endpoints) with the Substance or relying on using grouping and read-across approaches.

13 We have identified the following issue(s) with the proposed scope of the grouping:

0.2.1.1. Incomplete description of the applicability domain of the category

14 A category (grouping) hypothesis should address "*the set of inclusion and/or exclusion rules that identify the ranges of values within which reliable estimations can be made for category members for the given endpoint*" (Guidance on IRs and CSA, Section R.6.2.4.1.). Particularly, the applicability domain identifies "*the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made*" (Guidance on IRs and CSA, Section R.6.2.1.2.). Therefore, to reliably predict properties within a category, the applicability domain should be described. Such description must cover the borders of the category, define unambiguous inclusion- and exclusion criteria, and must include a justification for these.

15 You describe the members of the category as substances belonging to the High Molecular Weight Phthalate Ester (HMWPE). However, you do not specify any applicability domain.

16 This applicability domain does not introduce unambiguous inclusion/exclusion criteria which would identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made for the (sub)category members.

0.2.1.2. Incomplete characterisation of target and source substances

17 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*".

18 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.).

19 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.

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

- Target: you specify that the Substance has a low probability of having significant ethyl branching and low levels of tetra-branched alkyl chains. In addition, you state that the backbone chain length of the Substance is expected to contain at least 9 carbon atoms. In the Figure1: Percent Primary Alcohol Backbone Length, you indicate that the Substance contains C9-C12 backbones.
- DIUP/Source substance 1: you specify that DIUP is more linear than the Substance and is expected to have less branches.
- L9-11P/Source substance 2: you specify that D911P is generated from "[redacted], in which the alkyl moieties have a carbon distribution of [redacted]% in the range C9 to C11, with following typical C-chain length distribution: C9: [redacted] %; C10: [redacted]% and C11: [redacted]%). In addition, you state that D911P is highly linear (minimum 80%) with predominantly mono-2-methyl branching in the reminder, and is expected to have less branches than the Substance
- DIDP/Source substance 3: you specify that DIDP is generated from a C10 [redacted] which is C10 rich and some C8, C9 and C11 isomers. In addition, you state that DIDP is expected to have a similar level and type of branching as the Substance with alkyls of a shorter chain length than the Substance. In the Figure1: Percent Primary Alcohol Backbone Length, you indicate that DIDP contains C7-C9 backbones.
- DINP/Source substance 4:you specify that DINP is generated from an [redacted] and contains mainly C9- branched isomers and C9-10 branched isomers. In the Figure1: Percent Primary Alcohol Backbone Length, you indicate that DIDP contains C6-C8 backbones.
- DIDP/Source substance 5: In 'Figure 2: Developmental and Reproductive Summary Figure', you indicate that DIDP contains C7-C9 backbones.
- DUDP/Source substance 6: You state that "*… (DUDP; CAS 3648-20-2)… is described as having over [redacted]% a straight ester side chain of eleven carbons, and with some methyl C10 branched material (total carbon number (C11), mainly C11 with some C10 backbone). DUDP shares the same number of carbons in the alkyl chain as the registered substance with overlap of the longest linear carbon chain lengths. This substance overlaps the registered substance and brackets the high end of the alkyl chain analogue read across*". In 'Figure 1: Percent Primary Alcohol Backbone Length' and 'Figure 2: Developmental and Reproductive Summary Figure', you indicate that DUDP contains C10-C11 backbones.

- DnOP/Source substance 7: In 'Figure 1: Percent Primary Alcohol Backbone Length', you indicate that DnOP contains C8 backbones

21 However, the target and source substances 1 to 7 listed above, you fail to provide a comprehensive description of the distribution of alkyl chain length and the branching of alkyl side carbon chain (i.e., isomeric composition) for the target and source substances supported by adequate scientific evidence.

22 In your comments to the draft decision you claim that the composition of the registered substance is fully described in an attachment to your IUCLID dossier. ECHA acknowledges that IUCLID Section 1.4. includes a document entitled '[redacted]'. In this document, you provide an estimate of the relative amount of C11, C12, C13 and C14 isomers and of their branching index by GC analysis. You state that the Substance includes "*over 3000 isomers*" and that you could not determine their specific structure based on the analytical techniques available to you. You report that, based on NMR results, the average number of branches is 3.07. You state that "*based on experience, with a majority of di-branched alkyl chains and with low levels of mono and tera-branched, some tri-branched alkyl chains will be present*". Finally you claim that, to obtain adequate plasticizer performance in flexible PVC, "*it is absolutely critical to control the degree of branching of plasticizers and avoid highly branched plasticizers*".

23 ECHA maintains that the document referred to in your comments does not provide adequate information to precisely characterize the branching of alkyl side carbon chain (i.e., isomeric composition) as acknowledged by you in that document. In particular, while you claim that the Substance is expected to contain a maximum of 4 branches and 10 % of the branches as ethyl branches, the document does not provide evidence to demonstrate that constituents with a higher number of branches and/or longer branches than ethyl can be excluded.

24 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.

25 Despite of the above issues, ECHA understands that you rely on the category of "*high molecular weight phthalates (HMWPE)*" in order to meet the information requirements for the Substance, and your predictions are assessed on this basis.

0.2.2. Predictions for (eco)toxicological properties

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

0.2.2.1. Insufficient data density

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

28 According to the Guidance on IRs and CSA, Section R.6.2.1.5., one of the factors in determining the robustness of a category is the density and distribution of the available data across the category. To identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the category members needs to be available.

29 You have provided

- Short and Long-term terrestrial invertebrate studies on one category member (EC 271-090-9).

30 Information on few category members is not sufficient to establish a trend across broad category containing high molecular weight phthalates with carbon side chain backbone length of C6 and greater. Such information is not sufficient to cover the broad category of high molecular weight phthalates, considering wide variation in C-chain length and complex isomeric compositions, originating from branching of the side-chains. Therefore, the information provided is not sufficient to conclude that toxicological/ecotoxicological properties are likely to follow a regular pattern.

0.2.2.2. Missing supporting information to compare properties of the substances

31 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.).

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

33 For the source substances, you provide the studies used in the prediction in the registration dossier. Apart from that 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.

34 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.

35 In the new read-across approach provided in your comments to the draft decision, you invoke a "*phased bookend testing strategy*" for human health relying on the generation of additional supporting information on the Substance and on the analogue substances. You intend to conduct OECD 408-Sub-chronic 90-day studies on three substances (DIDP, DIUP and DTDP) "*to act as bridging studies to inform read-across hypothesis for skin sensitization, mutagenicity, reproductive and developmental endpoints*".

36 Your strategy relies essentially on data, which is yet to be generated, therefore no conclusion on the adequacy of the bridging information you intend to generate can currently be made.

0.2.2.1. Inadequate or unreliable studies on the source substances

37 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.
(3) cover an exposure duration comparable to or longer than the corresponding study that shall normally be performed for a particular information requirement if

exposure duration is a relevant parameter.

38 Specific reasons why the studies on the source substance(s) do not meet these criteria are explained further below under the requests 1, 2, 5, 6, 7, 11, 13 and 14. Therefore, no reliable predictions can be made for these information requirements.

0.2.3. Conclusion on the read-across approach

39 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. 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.

1.1. 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 (1982, 1985) with the source substance ditridecyl phthalate, EC 204-294-3 DTDP.

1.2. Assessment of the information provided

1.2.1. 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.

1.2.1.1. Inadequate or unreliable study on the source substance

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 mean number of revertant colonies per plate is reported for the treated doses and the controls;

c) 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 98 and TA 100 (i.e., the *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) is missing);

b) the mean number of revertant colonies per plate for the treated doses and the controls was not reported;

c) no repeat experiment was performed to confirm the negative results and no justification was provided.

45 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) required by the OECD TG 471.

46 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance. Therefore, your read-across approach under Annex XI, Section 1.5. is rejected.

47 Therefore, the information requirement is not fulfilled.

48 In the comments to the draft decision, indicate that you agree to perform the requested study.

1.3. Specification of the study design

49 To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471, 2020) is considered suitable.

2. Growth inhibition study aquatic plants

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

2.1. Information provided

51 You have provided:

(i) Growth inhibition study on aquatic algae performed according to USEPA 600/9-78-018, Printz Algal Assay (1997), with the Substance;

(ii) Growth inhibition study on aquatic algae, performed according to EU method C.3 (1993) with the source substance diisotridecyl phthalate, EC 248-368-3, CAS RN 27253-26-5.

52 In the comments to the draft decision, you have submitted:

(iii) QSAR prediction in accordance with Annex XI, Section 1.3, using the ester model from ECOSAR v.2.0.

2.2. Assessment of the information provided in the dossier

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

53 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.

2.2.2. Read-across adaptation rejected (study ii)

54 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.

2.2.2.1. Inadequate or unreliable study (ii) on the source substance

55 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed 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:

Technical specifications impacting the sensitivity/reliability of the test

a) for *Desmodesmus subspicatus* the initial cell density is 2-5 x10^3 cells/mL.

Characterisation of exposure

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

Reporting of the methodology and results

c) the test conditions are reported (*e.g.*, composition of the test medium, test temperature, test species, biomass density at the beginning of the test);

d) the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported. Algal biomass is normally determined based on dry weight per volume, or alternatively as cell counts or biovolume using microscopy or an electric particle counter. If an alternative method is used (*e.g.* flow cytometry, *in vitro* or *in vivo* fluorescence, or optical density), a satisfactory correlation with biomass must be demonstrated over the range of biomass occurring in the test;

e) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

56 In study (ii):

Technical specifications impacting the sensitivity/reliability of the test

a) The study (ii) was conducted on *Desmodesmus subspicatus* and the initial cell density was $2x10^4$ cells/mL;

Characterisation of exposure

b) Analytical monitoring was not conducted.

Reporting of the methodology and results

c) on the test conditions, you have not specified *e.g.*, composition of the test medium in the study (ii).

d) In study (ii), you report that algal biomass was determined photometrically at a wavelength of 685 nm. However, you have not reported evidence of correlation between the measured parameter and dry weight or cell numbers over the range of biomass occurring in the test;

e) tabulated data on the algal biomass determined daily for each treatment group and control are not reported

57 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the initial cell density used in the study (ii) is higher than specified for the species used and it may impact the sensitivity of the test. In addition, no analytical monitoring was performed to ensure the exposure to the test material was satisfactory.
- the reporting of the study (ii) is not sufficient to conduct an independent assessment of its reliability. More specifically, as you have not provided the information listed under point c) to e), 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 to assess the interpretation of the study results.

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

2.2.3. The provided study (i) does not meet the specifications of the test guidelines

59 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 based on the low water solubility (0.00000007 mg/L), adsorptive properties (Log K_{ow} > 5), and surface activity (30.9 mN/m). Therefore, the following specifications must be met:

Characterisation of exposure

a) adsorbing test substances, additional samplings for analysis at 24 hour intervals is required;

Reporting of the methodology and results

b) the test design is reported (*e.g.*, number of replicates, number of test concentrations and geometric progression used);

c) the test conditions are reported (*e.g.*, composition of the test medium, test temperature, test species, biomass density at the beginning of the test);

d) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;

e) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided;

f) as explained above 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.

60 In study (i):

Characterisation of exposure

a) the Substance is strongly adsorbing (Log K_{ow} >10, log K_{oc} >6), and no additional sampling for analysis at 24 h interval was conducted.

Reporting of the methodology and results

b) on the test design, you have not specified number of replicates.

c) on the test conditions, you have not specified *e.g.*, composition of the test medium and test temperature.

d) tabulated data on the algal biomass determined daily for each treatment group and control are not reported. In addition, you reported that "*Control chlorophyll a or cell counts were not reported*".

e) In study (i), on the analytical method adequate information, you have indicated that analytical monitoring was performed, and the detection limit of the analytical method was 0.10 mg/L, but the information on the method used and other performance parameters of the method is not reported.

f) the Substance is difficult to test, and you have not provided the information listed above.

61 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. In the absence of the above information, it is not possible to conduct an independent assessment as to whether the study (i) was conducted under conditions that are consistent with the specifications of the OECD TG 211, whether the validity criteria of the test guideline were met and whether the interpretation of the results is adequate.

62 On this basis, the specifications of OECD TG 201 are not met.

63 In the comments to the draft decision, you agree with ECHA's assessment.

2.3. Assessment of the information provided in the comments

2.3.1. (Q)SAR adaptation (study iii) rejected

64 Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

(1) results need to be adequate for the purpose of risk assessment or classification and labelling, and
(2) adequate and reliable documentation of the method must be provided.

65 Regarding these conditions, we have identified the following issue:

2.3.1.1. Lack of justification of the representativeness of the structures

66 Under Guidance on IRs and CSA R.6.1.7.3. a prediction is adequate for the purpose of classification and labelling and/or risk assessment if the following conditions are met:

- the composition of the substance is clearly defined, and
- representative structure(s) for the assessment are selected.

67 Your registration dossier provides the following information:

- In Section 1.1. of your technical dossier, you define the Substance as an UVCB;
- In Section 1.2., you indicate that the Substance contains a high number of (unknown) branched isomers;

68 You provided predictions for the following structure:

- O=C(c1ccccc1C(=O)OCCC(C)CC(C)CC(C)CCC)OCCC(C)CC(C)CC(C)CCC

69 As already explained in the Section 0.1.1.2., you state that the Substance contains over 3000 isomers but you do not provide detailed compositional information of the Substance (including information on isometric composition). Therefore, the Substance cannot be regarded as a well-defined substance.

70 In your comments, you state that "*due to its extremely low water solubility (ca. 0.0007 µg/L), adsorptive properties (log Kow 12)*", no effects are expected at saturation. According to you, this is because above certain limits (i.e. logKow ≥5.0 for fish/ daphnia, logKow ≥ 6.4 for algae for acute effects, and logkow≥8 for chronic effects), empirical data indicate that the decreased solubility of lipophilic chemicals results in "*no effects at saturation*". ECHA acknowledges your comment. However, the Substance contains constituents of varying carbon chain length as well as isomers with varying degree of branching. Lower carbon-chain length and higher branching both lead to higher solubility and reduced lipophilicity. On this basis, you have not provided adequate justification that the selected structure (C11 including three methylation) and the log Kow estimate for the Substance (i.e., 12) are representative of the Substance as a whole (including its isomers with lower carbon number / higher degree of branching). On this basis, you fail to provide a justification as to why the selected structure can be regarded as representative of the Substance as a whole.

Therefore, you have not demonstrated that the prediction is adequate for the purpose of classification and labelling and/or risk assessment and your adaptation is rejected.

71 Therefore, the information requirement is not fulfilled.

2.4. Study design and test specifications

72 The Substance is difficult to test due to the low water solubility (0.00000007 mg/L), adsorptive properties (Log K_{ow} > 5), and surface activity (30.9 mN/m). 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.

73 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).

74 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

75 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.

3.1. Triggering of the information requirement

76 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.

77 You have provided the water solubility of the Substance to be 0.00000007 mg/L at 25 °C, calculated based on the quantitative structure-property relationship (QSPR) three-solubility model.

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

3.2. Information requirement not fulfilled

79 The information provided, its assessment and the specifications of the study design are addressed under request 7.

Reasons related to the information under Annex VIII of REACH

4. In vitro gene mutation study in mammalian cells

80 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.

4.1. Triggering of the information requirement

81 Your dossier contains (I) an adaptation for in vitro gene mutation study in bacteria, and (II) a negative result for the in vivo micronucleus study.

82 The in vitro gene mutation study in bacteria provided in the dossier is rejected for the reasons provided in request 1.

83 The result of the request 1 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.

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

4.2. Information provided

85 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 mammalian cells (1986) with the source substance diundecyl phthalate, EC 222-884-9 DUP.

4.3. Assessment of the information provided

4.3.1. Read-across adaptation rejected

86 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.

87 Therefore, the information requirement is not fulfilled.

88 In the comments to the draft decision, you agree to perform the requested study.

4.4. Specification of the study design

89 To fulfil the information requirement for the Substance depending on the result of the request 1, either the in vitro mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

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

90 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.

5.1. Information provided

91 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 21-day sub-acute toxicity oral study (1986, report number [redacted]) with the source substance Di-isodecyl phthalate, no EC nor CAS provided;

(ii) a 28-day sub-acute toxicity oral study (1990, Report number [redacted]) with the source substance Di-isodecyl phthalate; bis(7,7-dimethyloctyl) phthalate, EC 247-977-1;

(iii) a 10-days sub-acute toxicity inhalation study (1981, Report number [redacted]) with the source substance bis(8-methylnonyl) phthalate, EC 271-091-4;

(iv) a 6 week short-term repeated dose toxicity dermal study (1969) with the source substance bis(7-methyloctyl) phthalate, EC 271-090-9, DINP.

5.2. Assessment of the information provided

5.2.1. Read-across adaptation rejected

92 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 issues addressed below.

5.2.1.1. Inadequate or unreliable studies on the source substances

93 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed and cover an exposure duration comparable to or longer than the one specified in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 407. Therefore, the following specifications must be met:

a) testing is performed with at least three dose levels (unless conducted at the limit dose) and with concurrent controls;

In study (iv) only one dose level was described.

b) at least 5 male and 5 female animals are used for each concentration and control group;

In study (ii) only males were included in each test and control group.

In study (iv) only 4 males and 4 females were included in each test and control group.

c) dosing of the test substance is performed daily for a minimum of 28 days;

In study (i) the exposure duration was only 21 days.

In study (iii) the exposure duration was only 10 days.

d) haematological and clinical biochemistry tests are performed as specified in paragraphs 32-39 of OECD TG 407;

In studies (i and ii) the following haematology investigations were missing: haematocrit, haemoglobin concentrations, erythrocyte count, reticulocytes,

total and differential leucocyte count, platelet count and a measure of blood clotting time/potential.

In study (i) the following clinical biochemistry investigations were missing: sodium, potassium, glucose, urea, creatinine, total protein and albumin, and bile acids

e) full histopathology, including incidence and severity, is performed as specified in paragraphs 47-49 of OECD TG 407.

In studies (i and ii) the following histopathology items were not reported: ovaries, epididymides, prostate and seminal vesicle, uterus, adrenal, thyroid, vagina.

In study (iv) the following histopathology items were not studied: spleen, adrenals, heart (as specified in the OECD TG 407 available at the time of the study).

94 Therefore, the studies submitted in your adaptation, as currently reported in your dossier, do not provide an adequate and reliable coverage of the key parameter(s) of the corresponding OECD TG (studies i, ii, and iv) and do not cover an exposure duration comparable to or longer than the one specified in the corresponding OECD TG (study i and iii).

5.2.1.2. Study not conducted by the most appropriate route (study iv)

95 According to the 'Guidance on IRs and CSA, Section R.7.5.4.3.2.', the default route is oral. However, the dermal or the inhalation route may be more appropriate, depending on the physico-chemical properties of the Substance, the most relevant route of human exposure, and other toxicological considerations.

96 Under Annex VIII, Section 8.6.1., Column 2, Paragraph 2, the appropriate route shall be chosen on the following basis:

97 Testing by the dermal route is appropriate if:

- inhalation of the substance is unlikely, and
- skin contact in production and/or use is likely, and
- the physicochemical and toxicological properties suggest potential for a significant rate of absorption through the skin.

98 The study (iv) was performed with exposure via the dermal route. According to IUCLID section 7.1.2., dermal absorption is very low. You did not provide a justification for the choice of the dermal route of exposure. You have not demonstrated that the dermal route is the most appropriate route of exposure.

99 The oral route is the most appropriate route, as neither the criteria listed above for the dermal route are met.

100 Based on the above, the provided study (iv) is not performed according to the appropriate route.

101 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance.

102 Therefore, the information requirement is not fulfilled.

5.2.1.3. Incomplete information on the identity of the test material

103 Under Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment.

104 In order to predict the properties of the Substance, the test material used in the study on the source substance must be representative for the source substance (Article 10 and Recital 19 of REACH; Guidance on IRs and CSA, Section R.4.1.). Therefore, the unambiguous characterisation of the composition of the test material used to generate the source data is required to assess whether the test material is representative for the source substance.

105 You have identified the test material as Di-isodecyl phthalate (study i), without further information, including composition of the test material.

106 In the absence of the information on the composition, impurities of the test material, you have not demonstrated that the test material is representative for the source substance. Therefore, the study is not adequate for the purpose of classification and labelling and/or risk assessment.

107 Therefore, the information requirement is not fulfilled.

5.3. Specification of the study design

108 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, because no inhalation specific effects are assumed based on available information. In addition, the Substance is not respirable (low vapour pressure), and there is no data showing that dermal exposure is more toxic than oral.

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

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

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

111 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 6).

112 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.

113 In case the adopted decision no longer contains a request for a 90-day study, you are required to provide a 28-day study.

114 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 6; or
- a 28-day study as per the study design described in 5.3 in case the 90-day study is not requested in the adopted decision.

115 In the comments to the draft decision, you indicate that *"an adaptation for the short-term repeated dose toxicity has been added to the registered substance dossier and provided in attachment"*. However, the information is currently still not available in your registration dossier. Therefore, the data gap remains. You must submit this information in an updated registration dossier by the deadline set in the decision.

Reasons related to the information under Annex IX of REACH

6. Sub-chronic toxicity study (90 days)

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

6.1. Information provided

117 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 (1968) with the source substance Di-isodecyl phthalate, no EC no CAS provided, DIDP.

6.2. Assessment of the information provided

6.2.1. Read-across adaptation rejected

118 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 issues addressed below.

6.2.1.1. Inadequate or unreliable study on the source substances

119 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.

120 In study (i):

a) oestrus cyclicity was not assessed.

121 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.

122 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance. Therefore, your read-across approach under Annex XI, Section 1.5. is rejected.

Therefore, the information requirement is not fulfilled.

6.2.1.2. Incomplete information on the identity of the test material

123 Under Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment.

124 In order to predict the properties of the Substance, the test material used in the study on the source substance must be representative for the source substance (Article 10 and Recital 19 of REACH; Guidance on IRs and CSA, Section R.4.1.). Therefore, the

unambiguous characterisation of the composition of the test material used to generate the source data is required to assess whether the test material is representative for the source substance.

125 You have identified the test material as Di-isodecyl phthalate, without further information, including composition of the test material.

126 In the absence of the information on the composition, impurities of the test material, you have not demonstrated that the test material is representative for the source substance. Therefore, the study is not adequate for the purpose of classification and labelling and/or risk assessment.

127 Therefore, the information requirement is not fulfilled.

128 In the comments to the draft decision, you agree to perform the requested study.

6.3. Specification of the study design

129 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.

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

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

7. Pre-natal developmental toxicity study in one species

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

7.1. Information provided

133 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on the following:

(i) a pre-natal developmental toxicity study in rodents (mice) (1987), with the source substance 1,2-benzenedicarboxylic acid, di-isodecyl ester, EC 247-977-1, CAS RN 26761-40-0;

(ii) a pre-natal developmental toxicity study in rodents (rats) (1995 and 1999), with the source substance 1,2-Benzenedicarboxylic acid di-C9-11-branched alkyl esters, C10-rich, EC 271-091-4, CAS RN 68515-49-1;

(iii) a pre-natal developmental toxicity study in rodents (rats) (1997), with the source substance 1,2-Benzenedicarboxylic acid di-C9-11-branched alkyl esters, C10-rich, EC 271-091-4, CAS RN 68515-49-1;

(iv) a pre-natal developmental toxicity study in rodents (rats) (2013), with the source substance Di tridecyl phthalate, EC 204-294-3; CAS RN 119-06-2;

(v) a pre-natal developmental toxicity study in rodents (rats) (2001), with the source substance 1,2-Benzenedicarboxylic acid, di-C9-11-branched and linear alkyl esters, EC 271-083-0, CAS RN 68515-41-3 and 1,2-Benzenedicarboxylic acid di-C9-11-branched and linear alkyl esters, EC 271-085-1, CAS RN 68515-43-5;

(vi) a pre-natal developmental toxicity study in rodents (rats) (2011), with the source substance dioctyl phthalate, EC 204-214-7, CAS RN 117-84-0;

7.2. Assessment of the information provided

7.2.1. Weight of evidence adaptation rejected

134 Annex XI, Section 1.2. states that there may be sufficient weight of evidence from several independent sources of information enabling, through a reasoned justification, a conclusion on the information requirement, while the information from each single source alone is insufficient to fulfil the information requirement.

135 The justification must have regard to the information that would otherwise be obtained from the study that must normally be performed for this information requirement.

136 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude on the corresponding information requirement.

7.2.1.1. Lack of documentation justifying the weight of evidence adaptation

137 Annex XI, Section 1.2. requires that adequate and reliable documentation is provided to describe a weight of evidence approach. This documentation must include robust study summaries of the studies used as sources of information and a justification explaining why the sources of information together provide a conclusion on the information requirement.

138 You have not included a justification for your weight of evidence adaptation for this information requirement, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude on the information requirements under consideration.

139 In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation.

140 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.7.2 at Annex IX includes similar information that is produced by the OECD TG 414 on one species. The following aspects are covered: 1) prenatal developmental toxicity, 2) maternal toxicity, and 3) maintenance of pregnancy.

7.2.1.2. Pre-natal developmental toxicity

141 Pre-natal developmental toxicity includes information after pre-natal exposure on embryonic/foetal survival (number of live foetuses; number of resorptions and dead foetuses, post implantation loss), growth (body weights and size) and structural malformations and variations (external, visceral and skeletal).

142 Studies (ii, iv, v and vi) may provide relevant information on pre-natal development. The RSS you have provided for study (i) does not specify if and to what extent pre-natal development was studied. Study (iii) may provide limited relevant information on pre-natal development, but does not inform on external, visceral, or skeletal alterations.

7.2.1.3. Maternal toxicity

143 Maternal toxicity includes information after gestational exposure on maternal survival, body weight and clinical signs and other potential aspects of maternal toxicity in dams.

144 Studies (ii, iii, iv, v and vi) may provide relevant information on maternal toxicity. The RSS you have provided for study (i) does not specify if and to what extent maternal toxicity was studied.

7.2.1.4. Maintenance of pregnancy

145 Maintenance of pregnancy includes information on abortions and/or early delivery as a consequence of gestational exposure and other potential aspects of maintenance of pregnancy.

146 Studies (ii, iv, v and vi) may provide relevant information on the maintenance of pregnancy. The RSS you have provided for study (i) does not specify if and to what extent the maintenance of pregnancy was studied. Study (iii) may provide limited relevant information on the maintenance of pregnancy, but does not inform on the number of animals aborting or delivering early, or the number and percent of pre- and post-implantation losses.

147 However, the reliability of these sources of information is significantly affected by the following deficiencies:

7.2.1.5. Read-across adaptation rejected

148 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.

149 In addition, ECHA identified the following deficiencies which also affect significantly the reliability of the sources of information.

7.2.1.5.1. The provided studies (i), (iii) and (vi) do not meet the specifications of the test guideline

150 The property investigated shall normally result from a study performed in accordance with OECD TG 407. This guidance includes the following specifications:

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

b) at least 20 female animals with implantation sites for each test and control group are included;

c) the exposure duration is at least from implantation until one day prior to scheduled caesarean section;

d) the study is conducted in rats or rabbits;

151 The reported data for the studies you have provided did not include:

a) only one dose level was included in study (i);

b) the number of females used in each test and control group is not specified in studies (iii) and (vi);

c) the exposure duration was limited to GD6-GD13 in study (i); The exposure duration was limited to GD6-GD15 in study (iii); in study (vi) the duration of exposure is not specified;

d) the study was conducted in mice without justification study (i);

152 In summary, the source of information (i) has a critical reliability issue with regard to insufficient number of doses used, insufficient exposure duration, and the unjustified use of non-rat species. These issues make the presented results unreliable, because it is impossible to make considerations related to dose-response, not all potential adverse outcomes are covered due to the limited exposure duration, and species-specific effects may affect the outcome, respectively. With regards to studies (iii) and (vi), not having any

data on the number of animals used is a critical reliability issue, as this information is required to assess the statistical power of the study.

153 In the absence of such information on critical aspects of the specifications of the provided studies, ECHA cannot evaluate the reliability of the conclusions on the pre-natal developmental toxicity.

154 Therefore, the studies you have provided in your adaptation, as currently reported in your dossier, do not provide and adequate and reliable coverage of the key parameters of the corresponding OECD TG.

7.2.1.6. Conclusion

155 It is not possible to conclude, based on any of the new sources of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in OECD TG 414.

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

157 In the comments to the draft decision, you agree to perform the requested study.

7.3. Specification of the study design

158 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species.

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

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

8. Long-term toxicity testing on aquatic invertebrates

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

8.1. Information provided

162 You have provided:

(i) a long-term toxicity study on *Daphnia magna,* performed according to EPA 560/6-82-002 (1995), with the Substance;

(ii) a long-term toxicity study on *Daphnia magna*, performed according to OECD TG 211 (1998), with the Substance.

8.2. Assessment of the information provided

8.2.1. Test material in studies (i) and (ii) not representative of the Substance

163 As explained in Section 0.1., the test material in studies (i) and (ii) is not representative of the Substance.

164 In your comment to the draft decision, you state that:

- study (i) was performed with a test substance which was a blend of three commercial products, including the Substance. You state that the details of the test material data

(e.g. source, purity, analytical characterisation of the test material) will be added to the study record;

- the information on the feedstock and manufacturing process support that the test material was representative of the Substance in study (ii).

165 ECHA acknowledges your intention to clarify the identity of the test materials used in studies (i) and (ii). However, as you have not provided this information in your comments to the draft decision, no assessment can be made. Therefore, the deficiency remains.

166 In addition, ECHA identified the endpoint-specific issue addressed below.

8.2.1.1. The provided studies do not meet the specifications of the test guidelines

167 To fulfil the information requirement, a study must comply with the OECD TG 211 and the specifications of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Reporting of the methodology and results

a) the test procedure is reported (e.g. loading in number of *Daphnia* per litre, test medium composition, identity and quantity of the vehicle used);

b) the nominal test concentrations and the results of all analyses to determine the concentration of the test substance in the test vessels are reported;

c) water quality monitoring within the test vessels (i.e. TOC and/or COD) is reported;

d) the full record of the daily production of living offspring during the test by each parent animal/in each replicate is provided;

e) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided;

f) As explained above, the Substance is difficult to test. Therefore the following additional information must be provided:

- the results of a preliminary solubility and stability studies,
- a description of the methods used to prepare stock and test solutions, and
- if the test material is tested at the saturation concentration, evidence that all reasonable efforts have been taken to achieve a saturation concentration.

168 In studies (i) and (ii):

Reporting of the methodology and results

a) You have not reported any of the information in the study (i).

b) the nominal test concentrations and the results of all analyses to determine the concentration of the test substance in the test vessels are not reported in the study (i).

c) water quality monitoring within the test vessels (TOC and/or COD) are reported in in neither studies (i) nor (ii).

d) the full records of the daily production of living offspring during the test by each parent animal (semi-static test) in the study (ii) / in each replicate (flow-through test) in study (i) are not reported.

e) on the analytical method adequate information, including performance parameters of the method, is reported in neither studies (i) nor (ii).

f) No information is provided in the studies (i) and (ii).

169 In your comment to the draft decision, you point out that both studies (i) and (ii) are performed prior to the first edition of OECD GD 23. You state that both studies, nevertheless employed the methods to address challenges of testing poorly water soluble test substances.

170 In addition, for the study (ii), you provide justification for the use of the vehicle and for the interpretation of the results, which can be summarised as below:

- Although OECD GD 23 does not general recommend the use of vehicle, the presence of non-dissolved test material poses difficulty for the determination of exposure concentrations, as well as, potentially exert physical effects which is not related to toxicity of the test material;
- The concentration of the vehicle applied is according to the TG and OECD TG 202 (part II) allowed for the use of vehicle if it does not exceed 100 mg/L;
- The use of vehicle and loading above solubility limit of the test material allowed for a stable dispersion at maximum dissolved concentration in the solution;
- No significant difference in the key parameters is observed between the control, treatment or the vehicle control;
- There was no significant difference in survival, growth or reproduction between the control, treatment, or dispersant control.

171 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, your comments to the draft decision partially address the issue f). However, provided information still does not demonstrate that the exposure concentration of the test material was maximised in the test solution, and as you still do not provide the information listed under point a) to e), 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 requirements of the OECD TG 211 and OECD GD 23, and to assess the interpretation of the study results.

172 In your comments, you argue that results from the study (ii) supports that no toxic effect are to be seen up to saturation. As both studies (i) and (ii) consistently demonstrate that the Substance does not elicit chronic toxicity to aquatic invertebrates at saturation concentration, you consider that the information requirements are fulfilled. However for the reasons explained above, the validity of results of the studies cannot be confirmed.

173 Therefore, the information provided in your comments does not change the assessment outcome. You remain responsible for complying with this decision by the set deadline.

174 On this basis, the specifications of OECD TG 211 are not met.

175 Therefore, the information requirement is not fulfilled.

8.3. Study design and test specifications

176 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.

9. Long-term toxicity on terrestrial invertebrates

177 Short-term toxicity to invertebrates is an information requirement under Annex IX to REACH (Section 9.4.1). Long-term toxicity testing must be considered (Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

9.1. Triggering of the information requirement

178 Under Annex IX, Section 9.4., column 2, for substances that have a high potential to adsorb to soil or that are very persistent, long-term toxicity testing must be considered instead of short-term. Guidance on IRs and CSA, Section R.7.11.5.3. clarifies that a substance is considered to be very persistent in soil if it has a half-life >180 days. In the absence of specific soil data, high persistence is assumed unless the substance is readily biodegradable.

179 Based on the information from your registration dossier, the Substance is considered to have high adsorption potential to soil, as you report predicted log 29now above 5 for the Substance.

180 Therefore, the Substance has a high potential to adsorb to soil. On this basis, information on long-term toxicity on terrestrial invertebrates must be provided.

9.2. Information requirement not fulfilled

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

10. Effects on soil micro-organisms

182 Effects on soil microorganisms is an information requirement under Annex IX to REACH (Section 9.4.2).

10.1. Information provided

183 Furthermore, you have adapted this information requirement and provided a justification which ECHA understand is an adaptation under Annex IX, Section 9.4., Column 2. To support the adaptation, you have provided following justification:

184 "*In accordance with REACH Chapter R.7C Endpoint Specific Guidance, specifically R.7.11.6.3 Testing Strategy (Table R.7.11-2), data to characterize toxicity to soil microorganisms is waived for the following reasons. DTDP is biodegradable, consequently it is considered to degrade rapidly in the environment and not persist. DTDP does not cause acute or chronic aquatic toxicity at its maximum water solubility, consequently it does not pose an acute or chronic aquatic hazard, and it is not possible to derive NOEC or PNEC values needed for quantitative risk assessment. However, it is possible to qualitatively conclude based on low solubility and available effects test data that DTDP is not harmful to aquatic organisms. Acute and chronic toxicity data for soil macro-organisms, earthworms, also show that DTDP does not cause effects at high soil loading rates. Data also show that analogues of DTDP do not inhibit respiration in wastewater treatment microorganisms at levels above its water solubility. Therefore, based on these considerations, additional short and long-term toxicity testing for soil microorganisms is not needed*".

10.2. Assessment of the information provided

10.2.1. The adaptation under Annex IX, Section 9.4., column 2 is rejected

185 Under Annex IX, Section 9.4., column 2, in the absence of toxicity data to soil organisms, the equilibrium partitioning method (EPM) may be applied to assess the hazard to soil organisms. In this context, the Guidance on IRs and CSA, Section R.7.11.6. describes an integrated testing strategy (ITS) for Effects on Terrestrial Organisms. This approach relies on the assignment of the Substance to a "soil hazard category" and on an initial screening assessment using the EPM, in order to decide the information needed for the chemical safety assessment.

186 As explained under the requests 2, 3 and 8, the information in your dossier does not allow to conclude on the aquatic toxicity of the Substance. Therefore, it is not possible to assign the Substance to any "Soil hazard category" and the initial screening assessment using the EPM it is not applicable.

187 Therefore, you have not demonstrated that this information can be omitted and the information requirement is not fulfilled.

188 In the comments to the draft decision, you agree to perform the requested study.

10.3. *Study design and test specification*

189 ECHA Guidance R.7.11.3.1. specifies that Soil Microorganisms: Nitrogen Transformation Test (EU C.21/OECD TG 216) is considered suitable for assessing long-term adverse effects on soil microorganisms for most non-agrochemicals.

11. Long-term toxicity on terrestrial plants

190 Short-term toxicity plants is an information requirement under Annex IX to REACH (Section 9.4.3). Long-term toxicity testing must be considered (Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

11.1. Triggering of the information requirement

191 As already explained under request 9 above, information on long-term toxicity study must be provided as the Substance is considered to have high adsorption potential to soil.

11.2. Information requirement not fulfilled

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

Reasons related to the information under Annex X of REACH

12. Pre-natal developmental toxicity study in a second species

193 Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is an information requirement under Annex X, Section 8.7.2.

12.1. Information provided

194 You have not submitted any information for this requirement.

195 Therefore, the information requirement is not fulfilled.

196 In the comments to the draft decision, you agree with ECHA's assessment. You "plan to decide how to address this endpoint (read across vs experimental study) in a phased approach to testing".

197 ECHA takes note of your intentions. You remain responsible for complying with this decision by the set deadline.

12.2. Specification of the study design

198 A PNDT study according to the test method OECD TG 414 should be performed in rabbit or rat as preferred second species, depending on the species tested in the first PNDT study (request 7 in this decision).

199 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex X, Section 8.7.2., Column 1).

200 Based on the above, the study must be conducted in rabbits or rats with oral administration of the Substance.

13. Long-term toxicity testing on terrestrial invertebrates

201 Long-term toxicity to terrestrial invertebrates is a standard information requirement in Annex X to REACH (Section 9.4.4.).

13.1. Information provided

202 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 from the source substances:

(i) a long-term toxicity testing on invertebrates, performed according to OECD TG 222 (2009), with the source substance 1,2-benzenedicarboxylic acid, di-C8-C10-branched alkyl esters, C9 Rich, EC 271-090-0, CAS NR 68515-48-0.

203 In addition, you provided the same justification as in the effect on soil micro-organisms (request 10 above) according to which you consider that "additional short and long-term toxicity testing for soil organisms is not needed".

13.2. Assessment of the information provided

13.2.1. Read-across adaptation rejected

204 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 issues addressed below.

13.2.2. The adaptation under Annex X, Section 9.4., column 2 is rejected

205 As explained under the request 10, your adaptation is rejected.

206 Therefore, the information requirement is not fulfilled.

207 In the comments to the draft decision, you agree to perform the requested study.

13.3. Study design and test specification

208 ECHA Guidance R.7.11.3.1. specifies that the earthworm reproduction test (OECD TG 222), the Enchytraeid reproduction test (OECD TG 220), and the Collembolan reproduction test (OECD TG 232) are appropriate to cover the information requirement for long-term toxicity testing on terrestrial invertebrates. ECHA is not in a position to determine the most appropriate test protocol since this decision is dependent upon species sensitivity and substance properties. However, when log Kow >5 and log Koc >4, as in this case, the test OECD 232 is not appropriate as the dominant route of exposure for Collembolans is via pore water.

14. Long-term toxicity testing on terrestrial plants

209 Long-term toxicity to plants is a standard information requirement in Annex X to REACH.

14.1. Information provided

210 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 from the source substances:

(i) a long-term toxicity to terrestrial plants, performed according to OECD TG 208 (1995), with the source substance diidotridecyl phthalate, EC 248-368-3, CAS NR 27253-26-5; and
(ii) a short-term to terrestrial plants, performed according to EPA600/3-88/029 (1996), with the source substance, DIDP, EC 271-091-4, CAS RN 68515-49-1.

211 Furthermore, you have adapted this information requirement and provided a justification which ECHA understand is an adaptation under Annex X, Section 9.4., Column 2.

14.2. Assessment of the information provided

14.2.1. Read-across adaptation rejected

212 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.

14.2.1.1. The studies (i) and (ii) do not qualify for long-term studies

213 To fulfil the information requirement, a study must be a long-term toxicity on terrestrial plants.

214 For long-term toxicity testing, ECHA considers six species as the minimum to achieve a reasonably broad selection. Testing must be conducted with species from different families, as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD TG 208.

215 In the studies (i) and (ii), only three and two species respectively were tested.

216 The studies (i) and (ii) does not provide information on the long-term toxicity of the test material to the terrestrial invertebrates and they do not qualify as a long-term invertebrate tests. Therefore, this information is rejected.

14.2.2. Your adaptation based on exposure considerations is rejected.

217 Under Annex X, Section 9.4., Column 2 toxicity studies with soil organisms may be omitted if direct and indirect exposure of the soil compartment is unlikely.

218 In the registration dossier you report a number of various industrial, professional and consumer uses of the Substance including use in lubricating agent (outdoor) by professional users. There is no exposure assessment and risk characterisation reported in the chemical safety report.

219 Based on the uses identified in the registration dossier direct/ indirect (e.g. for outdoor uses of lubricants etc.) exposure of the soil cannot be ruled out. E.g. ECHA Guidance R.16 identifies worst-case release factor of 20% to soil for environmental release category (ERC) 8d which you assigned for use in lubricating agent. Furthermore, you have not reported any further justification (e.g. exposure assessment for soil compartment) which would support your adaptation on the basis of exposure considerations.

220 Your adaptation of information requirements on long-term toxicity to plants based on exposure considerations is therefore rejected.

221 Therefore, you have not demonstrated that this information can be omitted, and the information requirement is not fulfilled.

222 In the comments to the draft decision, you agree to perform the requested study.

14.3. *Study design and test specification*

223 The Terrestrial Plant Test (test method: OECD TG 208) is appropriate to cover the information requirement for long-term toxicity on terrestrial plants.

224 The OECD TG 208 considers the need to select the number of test species according to relevant regulatory requirements, and the need for a reasonably broad selection of species to account for interspecies sensitivity distribution. For long-term toxicity testing, ECHA considers six species as the minimum to achieve a reasonably broad selection. Testing must be conducted with species from different families, as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD TG 208.

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 an Extended One-Generation Reproductive Toxicity Study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. The EOGRTS may be addressed in a separate decision once the information from the sub-chronic toxicity study (90 days) requested in this decision is provided; because the results from the 90-day study are needed for the design of the EOGRTS. Similarly the information requirement for a screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) is not addressed in this decision; as the EOGRTS will cover the same parameters.

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.

This 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 to the draft decision, you requested an extension of the deadline to provide information from 36 to 48 months from the date of adoption of the decision.

You justify your request by possible delays due to limited capacity in the Contract Research Organizations (CRO). In addition, you argue that the extension is needed to proceed with the tiered testing strategy proposed by you in order to decide whether the request pre-natal study in rabbits can be covered by a read-across adaptation or whether a new study on the Substance should be conducted.

ECHA notes that you have not provided any documentary evidence to substantiate your request based on the limited capacity in the CRO. Secondly, the proposed tiered testing strategy relies on a read-across approach that has not yet been fully described and justified, as explained in in the Appendix on Reasons common to several requests above.

On this basis, ECHA has not modified the deadline to provide the information.

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

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

Appendix 3: Addressee(s) of this decision and their corresponding information requirements

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

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

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

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

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

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

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 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. 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.