~~Confidential~~

Helsinki, 24 May 2024

Addressees
Registrants of 215-553-5_1330-86-5_JS_EM Lead as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
01 July 2020

Registered substance subject to this decision ("the Substance")
Substance name: Diisooctyl adipate
EC/List number: 215-553-5

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***30 August 2027***.

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

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

1. Skin sensitisation (Annex VII, Section 8.3.)
   i. *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (OECD TG 442E) (Annex VII, Section 8.3.1.); and
   ii. only if the *in vitro/in chemico* test methods specified under point i.) above are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429)

2. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: OECD TG 471, 2020) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102

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

3. In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)

4. If negative results are obtained in tests performed for the information requirement of Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or 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 8. below, or, in case the sub-chronic toxicity study (90 days) is not requested: Short-term repeated dose toxicity (28 days) (Annex VIII, Section 8.6.1.) by oral route, to be combined with the screening for reproductive/developmental toxicity requested below

6. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats

7. Long-term toxicity testing on fish also requested below (triggered by Annex VIII, Section 9.1.3., column 2)

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

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

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

10. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210)

The reasons for the request(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

In the requests above, the same study has been requested under different Annexes or for different information requirements.

In the case of the same study 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.

In all cases, 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)

Reasons common to several requests

0.1. Read-across adaptation rejected

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

- Skin Sensitisation (Annex VII, Section 8.3)
- *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- *In vitro* micronucleus study (Annex VIII, Section 8.4.2.)
- *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.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study, one species (Annex IX, Section 8.7.2.)

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

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

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

0.1.1. Scope of the grouping of substances (category)

5 You provide a read-across justification document in IUCLID Section 13.

6 For the purpose of this decision, the following abbreviations are used for the source substance(s)/category members:

i. CAS 6938-94-9 / EC 230-072-0 / Diisopropyl adipate

ii. CAS 105-99-7 / EC 203-350-4 / Dibutyl adipate

iii. CAS 110-33-8 / EC 203-757-7 / Dihexyl adipate

iv. CAS 1330-86-5 / EC 215-553-5 / Diisooctyl adipate

v. CAS 123-79-5 / EC 204-652-9 / Dioctyl adipate

vi. CAS 103-23-1 / EC 203-090-1 / Bis(2-ethylhexyl) adipate (DEHA)

vii. CAS 68515-75-3 / EC 271-105-9 / Hexanedioic acid, di-C7-9-branched and linear alkyl esters

viii. CAS 33703-08-1 / EC 251-646-7 / Diisononyl adipate

ix. CAS 16958-92-2 / EC 241-029-0 / Bis(tridecyl) adipate

x. CAS 85117-94-8 / EC 285-645-8 / Bis(2-octyldodecyl) adipate

xi. CAS 103-24-2/ EC 203-091-7 / Bis(2-ethylhexyl) azelate

xii. CAS 897626-46-9 / EC 618-295-5 / Bis(2-octyldodecyl) azelate

xiii. CAS 7491-02-3 / EC 231-306-4 / Diisopropyl sebacate

xiv. CAS 109-43-3/ EC 203-672-5 / Dibutyl sebacate

xv. CAS 122-62-3 / EC 204-558-8 / Bis(2-ethylhexyl) sebacate

xvi. CAS 69275-01-0 / EC not available / Bis(2-octyldodecyl) sebacate

7 You justify the grouping of the substances as:

8 "*Due to the structural similarities and consistent trend in physico-chemical, toxicological, ecotoxicological properties and toxicokinetic behaviour, the members of the PFAE linear group can be considered as a category of substances,…*"

9 You define the applicability domain as:

10 "*all members of the category PFAE linear are diester derivatives of the common saturated diacids: namely adipic (C6), azelaic (C9) and sebacic (C10) acid. The alcohol portion of the diesters generally falls in the C3-C20 carbon number range, including linear and branched alcohols*."

11 ECHA understands that this is the applicability domain of the grouping and your predictions are assessed on this basis.

0.1.2. Predictions for toxicological properties

12 You provide a read-across justification document in IUCLID Section 13.

13 You predict the properties of the Substance from information obtained from the following source substance(s): category member substances i., ii., iii, vi., viii., ix.

14 You provide the following reasoning for the prediction of toxicological properties:

15 "*Due to the structural similarities and consistent trend in physico-chemical, toxicological, ecotoxicological properties and toxicokinetic behaviour, the members of the PFAE linear group can be considered as a category of substances*,…"

16 You state the following prediction for the hazardous properties of the category members (including the Substance):

17 "*considering all available evidence and expert judgement the category members showed no acute oral, dermal or inhalation toxicity, no skin irritation, eye irritation or sensitizing properties, no human hazard for systemic toxicity after repeated oral, inhalative and dermal exposure and are not mutagenic or clastogenic and have shown no relevant reproduction toxicity and have no effect on intrauterine development*."

18 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

19 We have assessed this information and identified the following issue(s):

0.1.2.1. Read-across hypothesis contradicted by existing data

20 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 must 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.).

21 The observation of differences in the toxicological properties between the source substance(s) and the Substance would contradict the hypothesis that the properties of the Substance can be predicted from the data on the source substances. An explanation why such differences do not affect the read-across hypothesis must to be provided and supported by scientific evidence.

22 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar Substance and source substance(s) cause the same type of effect(s).

23 You predict no hazardous effects for the category substances but the study results related to skin sensitisation, repeated dose toxicity, mutagenicity, and reproductive/ developmental toxicity obtained with the source substance(s) vary and/or contradict your prediction for no hazardous effects.

0.1.2.1.1. Skin sensitisation

24 Positive results for skin sensitisation are observed in the Buehler study (OECD TG 406) conducted with the source substance ix. while negative results are reported for equivalent study (OECD TG 406) conducted for source substance ii.

0.1.2.1.2. Repeated dose toxicity

25 Test item related target organ toxicity effects are reported in

- a repeated dose 28-day oral toxicity study (OECD TG 407) conducted with the source substance vi. (increased renal and hepatic weight, hyaline and eosinophilic droplets in kidneys)

26 No test item related target organ toxicity effects are reported for a repeated dose 28-day oral toxicity study (OECD TG 407) with the source substance ii. and in the repeated dose 90 day oral toxicity study (OECD TG 408) with the source substance vi.

0.1.2.1.3. Genotoxicity

27 In vitro cytogenicity study in mammalian cells with the source substance ii. reports a positive result.

0.1.2.1.4. Toxicity to reproduction or development

28 Test item related reproductive/developmental toxic effects are reported in

- a screening for reproductive/developmental toxicity study with the source substances ii. (reduction of pup viability) and vi. (litter losses in treated groups, mean litter size reduced)
- a prenatal developmental toxicity study with the source substance vi. (increase in pre-implantation loss and decreased litter size)
- a repeated dose 28-day oral toxicity study (OECD TG 407) conducted with the source substance vi. (increased ovarian follicle atresia and prolongation of the estrous stage)

0.1.2.1.5. Assessment outcome

29 The available set of data on the Substance and on the source substances indicates differences in the toxicological properties of the substances. This contradicts your read-across hypothesis whereby the Substance and source substances cause the same type of effect(s). However, you have not supported and scientifically justified why such differences in the toxicological properties do not affect your read-across hypothesis.

30 In your comments to the draft decision, you discuss the possibility of re-evaluating the outcome of your read-across adaptation Annex XI, section 1.5 (grouping of substances and read-across approach) in the future if the new data on Diisooctyl adipate (EC 215-553-5) and other adipates (such as Diisopropyl adipate EC 230-072-0, Diisotridecyl adipate EC 247-660-8, Diisononyl adipate EC 251-646-7) would demonstrate regular patterns (physchem, ecotox and tox) as a result of structural similarity.

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

0.1.2.2. Insufficient data density

32 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".

33 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.

34 You have provided:

- Skin sensitisation data obtained from either the guinea pig maximisation test and buehler test (OECD TG 406) for category members (source substances ii. and ix.);
- Repeated dose 28-Day oral toxicity study data (OECD TG 407) for two category members (source substances ii. and vi.);
- Repeated dose 90 day oral toxicity study data (OECD TG 408) for one category member (source substance vi.);
- In vitro gene mutation study in bacteria for three category members (source substances ii., iii., viii.);
- In vitro cytogenicity data using the in vitro mammalian chromosomal aberration test (OECD TG 473) for one category member (source substances ii.);
- In vitro gene mutation data obtained from the in vitro mammalian cell gene mutation tests using the Hprt and Xprt genes (OECD TG 476) for three category members (source substances i., vi. and viii.);
- Data for screening for reproductive/developmental toxicity obtained from either a reproduction/developmental toxicity screening test (OECD TG 421), or from an one-generation reproduction toxicity study (OECD TG 415) for two category members (source substances ii. and vi.), and
- Prenatal developmental toxicity study data (OECD TG 414) for one category member (source substance vi.).

35 Based on these studies you claim that "*the available data show similarities and trends within the category in regard to… toxicological properties*", and that "*for those individual endpoints showing a trend, the pattern in the changing of potency is clearly and expectedly related to the carbon chain length of the dicarboxylic acid and the carbon chain length and/or branching of the alcohol.*"

36 Information for three category members for skin sensitisation, two for 28-day repeated dose toxicity, one for 90-day toxicity, one for in vitro cytogenicity, three for in vitro gene mutation in mammalian cells, two for screening for reproductive/developmental toxicity, and one for developmental toxicity is not sufficient to establish a trend across the category consisting of 16 substances. Therefore, the information provided is not sufficient to conclude that toxicological properties are likely to follow a regular pattern.

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

37 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.).

38 Supporting information must include bridging studies to compare properties of the category members and information on the impact of exposure to the parent compounds on the prediction.

39 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar source substance(s) cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the source substance(s) is necessary to confirm that the substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

40 For skin sensitisation you have provided:

- a Guinea-pig maximisation study with the source substance ii.
- a Buehler study with the source substance ix.

41 No skin sensitisation information is available for the Substance or source substances i., iii., v., vi., vii., viii., x., xi., xii., xiii., xiv., xv. and xvi.

42 For repeated dose toxicity you have provided:

- a sub-acute toxicity study with the source substances ii. and vi.
- a sub-chronic toxicity study with the source substance vi.

43 No repeated dose toxicity information is available for the Substance or source substances i., iii., v., vii., viii., ix., x., xi., xii., xiii., xiv.

44 For mutagenicity you have provided

- *in vitro* gene mutation study in bacteria with the source substances ii., iii., viii.
- *in vitro* cytogenicity study with the source substance ii.
- *in vitro* gene mutation study in mammalian cells with the source substances i., vi., viii.

- *in vivo* mammalian erythrocyte micronucleus test with the source substances ii. and ix.

45 No mutagenicity information is available for the Substance or source substances v., vii., x., xi., xii., xiii., xiv., xv., xvi.

46 An in vitro gene mutation study in mammalian cells is considered complementary to a gene mutation study in bacteria and it is not intended to supersede the gene mutation study in bacteria as both studies investigate different mechanisms of gene mutation.

47 For reproductive/developmental toxicity you have provided

- a screening for reproductive/developmental toxicity study with the source substance ii.
- a developmental toxicity study with the source substance vi.

48 No reproductive toxicity information is available for the Substance or source substances i., iii., v., vii., viii., ix., x., xi., xii., xiii., xiv., xv., xvi.

49 Bridging studies of comparable design and duration for the Substance and of the source substances, as listed above are missing for skin sensitisation, repeated dose toxicity, mutagenicity and for reproductive/developmental toxicity. In the absence of such information, you have not established that the Substance and the source substances are likely to have similar properties.

50 Furthermore, end-point specific reasons why these studies cannot be considered reliable are explained further below under the requests 2 and 8.

51 Thus the data set reported in the technical dossier does not include relevant, reliable and adequate supporting information for the source substance(s) to support your read-across hypothesis.

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

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

53 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.

54 Specific reasons why the studies on the source substance(s) do not meet these criteria are explained further below under the applicable information requirement sections 2 and 8. Therefore, no reliable predictions can be made for these information requirements.

0.1.3. Conclusion

55 Based on the 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.

0.2. Weight of Evidence

56 Besides specifically claiming an adaptation using Annex XI, Section 1.5. (grouping of substances and read-across approach), you have indicated the adequacy of some of the endpoint study records as weight of evidence. Annex XI, section 1.2 (Weight of Evidence) requires that adequate and reliable documentation is provided to describe your weight of evidence approach. You have however not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/ assumption that the Substance has or has not a particular dangerous property. ECHA understands therefore you intend to adapt the information using Annex XI, Section 1.5. (grouping of substances and read-across approach) and has assessed the information on that basis.

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

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

1.1. Information provided

58 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 Buehler study type (1986) with the source substance ix;
(ii) a Guinea Pig Maximisation Study (1989) with the source substance ii.
(iii) Waiver justification "*An in vitro or in chemico skin sensitisation study does not need to be conducted because adequate data from an in vivo skin sensitisation study are available*."

1.2. Assessment of the information provided

1.2.1. Assessment whether the Substance causes skin sensitisation

1.2.1.1. Read-across adaptation rejected

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

60 Therefore, the studies (i) and (ii) do not allow to make a conclusion whether the Substance causes skin sensitisation.

1.2.1.2. In vitro or in chemico waiver justification rejected

61 As explained under 1.2.1.1., your read-across adaptation is rejected and as no information on the Substance is available, there is no basis for waiver justification (iii) either.

62 Your adaptation for in vitro or in chemico skin sensitisation study is therefore rejected.

1.2.2. No assessment of potency

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

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

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

1.3. Study design

66 To fulfil the information requirement for the Substance, information on molecular interaction with skin proteins and inflammatory response in keratinocytes and activation of dendritic cells (OECD TG 442C and OECD TG 442D and OECD TG 442E) must be provided.

Furthermore an appropriate risk assessment is required if a classification of the Substance as a skin sensitiser (Cat 1A or 1B) is warranted.

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

68 In your comments to the draft decision you propose performing a Weight of Evidence approach consisting of a combination of studies yet to be performed on the Substance (eg. GARDskin assay (OECD TG 442E) in combination with the OECD TG 442D) as the methods included in the currently adopted defined approaches are not suitable for your Substance, or results may lead to inconclusive prediction depending on the outcome of the tests. You indicated that the DPRA method included in OECD TG 442C is not suitable for UVCBs. ECHA notes that the DPRA method was updated in July 2023 to include gravimetric approach that allows testing UVCBs, therefore the Substance can be tested with that method.

69 ECHA acknowledges your proposed testing strategy, however depending on the outcome of the studies to be performed i.e. whether conclusion on classification and risk assessment can be obtained and the Column 2 conditions of Annex VII, Section 8.3.1. are fulfilled, revision of the approach may be needed. Therefore, it is your responsibility to consider whether conclusion on skin sensitisation potential and potency, if needed, can be obtained by the data generated as suggested in your comments. In case no firm conclusion can be made, additional testing, in vitro, or in vivo as last resort may be needed.

2. In vitro gene mutation study in bacteria

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

2.1. Information provided

71 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 (1996) with the source substance ii.;

(ii) an *in vitro* gene mutation study in bacteria (2012) with the source substance iii.

(iii) an *in vitro* gene mutation study in bacteria (1986) with the source substance viii.

2.2. Assessment of the information provided

2.2.1. Read-across adaptation rejected

72 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

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

73 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).

74 In study (iii) one of the required strains is not tested:

a) The test was performed with the strains *S. typhimurium* TA 1535, TA 1537, TA 1538, TA 98 and TA 100 (i.e., the fifth strain, either *S. typhimurium* TA102, *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101), is missing).

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

76 Therefore, the information requirement is not fulfilled.

77 In your comments to the draft decision, you agree with the request.

2.3. Study design

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

Reasons related to the information under Annex VIII of REACH

3. *In vitro* micronucleus study

79 An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is an information requirement under Annex VIII, Section 8.4.2.

3.1. Information provided

80 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* cytogenicity study in mammalian cells (1996) with the source substance ii.

(ii) an *in vivo* mammalian erythrocyte micronucleus test in mouse (2002) with the source substance ii.

(iii) an *in vivo* mammalian erythrocyte micronucleus test in mouse (1985) with the source substance ix.

3.2. Assessment of the information provided

3.2.1. Read-across adaptation rejected

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

82 Therefore, the information requirement is not fulfilled.

83 In your comments to the draft decision, you agree with the request.

3.3. Study design

84 According to the Guidance on IR & CSA, Section R.7.7.6.3., either the *in vitro* mammalian chromosomal aberration ("CA") test (test method OECD TG 473) or the *in vitro* mammalian cell micronucleus ("MN") test (test method OECD TG 487) can be used to investigate chromosomal aberrations in vitro. However, while the MN test detects both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the CA test detects only clastogenicity, as OECD TG 473 is not designed to measure aneuploidy (see OECD TG 473, paragraph 2).Therefore, you must perform the MN test (test method OECD TG 487), as it enables a more comprehensive investigation of the chromosome damaging potential in vitro. Moreover, in order to demonstrate the ability of the study to identify clastogens and aneugens, you must include two concurrent positive controls, one known clastogen and one known aneugen [1] (OECD TG 487, paragraphs 33 to 35).

3.3.1. Assessment of aneugenicity potential

85 If the result of the MN test is positive, i.e. your Substance induces an increase in the frequency of micronuclei, you must assess the aneugenic potential of the Substance.

86 In line with the OECD TG 487 (paragraph 4), you should use one of the centromere labelling or hybridisation procedures to determine whether the increase in the number of micronuclei is the result of clastogenic events (i.e. micronuclei contain chromosome fragment(s)) and/or aneugenic events (i.e. micronuclei contain whole chromosome(s)).

[1] According to the TG 487 (2016) "At the present time, no aneugens are known that require metabolic activation for their genotoxic activity" (paragraph 34).

4. *In vitro* gene mutation study in mammalian cells

87 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

88 Your dossier contains no data for *in vitro* gene mutation study in bacteria and for *in vitro* cytogenicity study in mammalian cells.

89 The result of the request 2 for information for an *in vitro* gene mutation study in bacteria and of the request 3 for an *in vitro* cytogenicity study in mammalian cells 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.

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

4.2. 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) an *in vitro* gene mutation study in mammalian cells (1988) with the source substance vi.

(ii) an *in vitro* gene mutation study in mammalian cells (1986) with the source substance viii.

(iii) an *in vitro* gene mutation study in mammalian cells (2013) with the source substance i.

4.3. Assessment of the information provided

4.3.1. Read-across adaptation rejected

92 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. Therefore, the information requirement is not fulfilled.

93 In your comments to the draft decision, you agree with the request.

4.4. Study design

94 To fulfil the information requirement for the Substance, 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-day)

95 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

96 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-acute toxicity study (1996) with the source substance ii.

(ii) a sub-acute toxicity study (2006) with the source substance vi.

5.2. Assessment of the information provided

5.2.1. Read-across adaptation rejected

97 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. Therefore, the information requirement is not fulfilled.

98 In your comments to the draft decision, you agree with the request.

5.3. Study design

99 When there is no information available neither for the 28-day repeated dose toxicity (EU B.7, OECD TG 407), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

100 The study design is addressed in request 6.3

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

101 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 8.3).

102 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.

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

104 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 8.3; or
- a 28-day study as per the study design described in 6.3. in case the 90-day study is not requested in the adopted decision.

6. Screening study for reproductive/developmental toxicity

105 A screening study for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1.

6.1. Information provided

106 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 screening study for reproductive/developmental toxicity (1996) with the source substance ii.

(ii) a one-generation reproduction toxicity study (1988) with the source substance vi.

6.2. Assessment of the information provided

6.2.1. Read-across adaptation rejected

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

108 In your comments to the draft decision, you agree with the request.

6.3. Study design

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

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

111 Therefore, the study must be performed in rats according to the OECD TG 421/422 with oral administration of the Substance.

112 In case the adopted decision no longer contains a request for a sub-chronic (90 days) study (e.g. as a result of an overall tonnage band change of the joint submission), a screening study for reproductive/developmental toxicity performed according to the OECD TG 422 is preferred.

113 When there is no information available neither for the 28-day repeated dose toxicity study (EU B.7, OECD TG 407), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

114 Under these circumstances, a study according to the test method EU B.64/OECD TG 422 must be performed in rats.

115 The information requirement for the 28-day repeated dose toxicity study is not fulfilled for the reasons explained under request 5.3.

7. Long-term toxicity testing on fish

116 Short-term toxicity testing on fish is an information requirement under Annex VIII, Column 1, Section 9.1.3. However, long-term toxicity testing on fish may be required by the Agency (Section 9.1.3., Column 2) if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

7.1. Triggering of the information requirement

117 In the provided OECD TG 105 (2011) study, the saturation concentration of the Substance in water was determined to be below the limit of detection of the analytical method (i.e. < 0.05 mg/L).

118 Therefore, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

7.2. Information requirement not fulfilled

119 The information provided, its assessment and the specifications of the study design are addressed under request 10.

Reasons related to the information under Annex IX of REACH

8. Sub-chronic toxicity study (90 days)

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

8.1. Information provided

121 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 (1982) in the rat with the source substance vi.

(ii) a sub-chronic toxicity study (1982) in the mouse with the source substance vi.

(iii) a one-generation reproduction toxicity studies (1988) with the source substance vi.

8.2. Assessment of the information provided

8.2.1. Read-across adaptation rejected

122 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issues addressed below.

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

123 Under Annex XI, Section 1.5., the study to be read across must have an adequate and reliable coverage of the key parameters addressed/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 408. Therefore, the following specifications must be met:

a) body weight and food consumption is measured at least weekly;

b) haematological and clinical biochemistry tests are performed as specified in paragraphs 30-38 of OECD TG 408

c) the oestrus cycle in females is examined at necropsy;

d) terminal organ and body weights are measured

e) gross pathological examinations as specified in paragraphs 43-46 of OECD TG 408

f) full histopathology is performed as specified in paragraphs 47-49 of OECD TG 408

g) The females should be nulliparous and non-pregnant.

124 In studies (i) and (ii):

a) there is no information on how frequently food consumption was measured;

b) haematology and clinical biochemistry were not performed;

c) oestrus cyclicity was not assessed;

d) terminal organ weights were not assessed and thus and organ/body weight ratios were not recorded;

e) data for organs for which the pathological examination was perfomed is missing

f) data for organs for which the histoppathological examination was perfomed is missing

In study iii):

b) haematology and clinical biochemistry were not performed

f) histopathology was performed on only on cervix, prostate, epididymis, seminal vesicle, liver, testis, mammary gland, uterus, ovary, abnormal tissues leaving out most of the tissues listed in paragraphs 43-46 of OECD TG 408

g) the animals were mated and females gave birth to offspring after pregnancy.

125 The information provided does not cover the specifications required by the OECD TG 408.

126 Based on the above, the studies do not provide an adequate and reliable coverage of the key parameters specified in the OECD TG 408. Therefore these studies are not an adequate basis for your read-across predictions.

127 In your comments to the draft decision, you agree with the request.

8.3. Study design

128 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.

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

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

9. Pre-natal developmental toxicity study in one species

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

9.1. Information provided

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

(i) a pre-natal developmental toxicity study in rat (1988) with the source substance vi.

9.2. Assessment of the information provided

9.2.1. Read-across adaptation rejected

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

134 Therefore, the information requirement is not fulfilled.

135 In your comments to the draft decision, you agree with the request.

9.3. Study design

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

137 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).

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

10. Long-term toxicity testing on fish

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

10.1. Information provided

140 In the registration dossier, you have adapted this information requirement and provided the following justification:

(i) You refer to the PFAE linear category and claim that short-term aquatic toxicity test results indicate no potential for aquatic toxicity for category members with the exception of two water soluble substances (source substance i. and ii., as listed under Section 0.1 of this Decision). In addition to this, you note that the PFAE linear category includes no long-term toxicity to fish studies.

(ii) You mention that members of the PFAE linear category are readily biodegradable and on this basis you claim that exposure of aquatic organisms is unlikely.

(iii) You refer to the ECHA Guidance on IRs and CSA, Chapter R.7b (ECHA, 2012b) which states that "*chronic fish toxicity testing is generally only necessary, when the P and B criteria are fulfilled*" and claim that the Substance does not fulfil the P and B criteria.

(iv) You mention animal welfare.

10.2. Assessment of information provided in the registration dossier

141 Regarding your justification under point (i), we have identified the following issue.

142 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. As explained above in request 7, the Substance is poorly water soluble.

143 In addition to this, short-term fish studies (in this case, OECD TG 203 studies) cover different investigations than the ones that are needed to fulfil the long-term toxicity testing on fish information requirement (in this case, the investigations of OECD TG 210).

144 Because of these reasons, the finding that shows a lack of toxicity for a poorly water soluble substance in a short-term aquatic toxicity study cannot be used for excluding that the same substance will show measurable toxic effects in a long-term study.

145 As you have stated in your justification, the PFAE linear category includes no long-term toxicity to fish studies. Because of this, adapting the information requirement by referring to this category is not possible.

146 Regarding your justification under points (ii) and (iii), we have identified the following issue.

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

147 A registrant may only adapt this information requirement based on the general rules set out in Annex XI.

148 It is noted that Column 2 of Annex IX, Section 9.1, does not allow omitting the need to submit information on long-term toxicity to fish under Column 1.

149 Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH and the legal basis you are relying on for your intended adaptation is not apparent to ECHA.

150 Regarding your justification under point (iv), we have identified the following issue.

10.2.2. Your justification regarding minimisation of vertebrate testing is rejected

151 Minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI or Annex IX, Section 9.1., Column 2.

10.3. Conclusion

152 Therefore, you have not demonstrated that this information can be omitted.

153 Therefore, the information requirement is not fulfilled.

10.4. Study design

154 To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (Guidance on IRs and CSA, Section R.7.8.2.).

155 The Substance is difficult to test due to the low water solubility (< 0.05 mg/L) and adsorptive properties: Log K_{ow} 8.12. OECD TG 210 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 210. 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.

156 In the comments to the draft decision, you provide the following information related to study design.

157 You mention that it is difficult to conduct an OECD TG 210 study for substances that have similar properties as the Substance (i.e. low solubility, high log Know, readily biodegradable), even if the approach described in OECD GD 23 is taken into account. Because of this, you propose to conduct an OECD TG 215 study instead. You quote OECD GD 23: "*For very poorly water soluble or highly hydrophobic test chemicals, a dietary exposure may be an ecologically relevant exposure route which can enable dose verification in chronic fish studies*" (Section 9, paragraph 176, footnote 11). On this basis, you propose to conduct an OECD TG 215 test with dietary exposure.

158 Guidance on IRs & CSA, Chapter R.7b, Section R.8.5.3 (ECHA, 2023) clarifies that while normally the OECD TG 210 would be considered appropriate for examining long-term fish toxicity, the fish juvenile growth test (OECD TG 215) may also be considered to fulfil the information requirement if the test substance has a log K_{ow} < 5 and there is no indication of endocrine disrupting properties or any other specific mode of action.

159 In section 4.7 of the registration dossier, you report that the log K_{ow} value of the Substance is 8.12.

160 On this basis, the fish juvenile growth test (OECD TG 215) is not considered to fulfil the information requirement for the Substance.

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

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 10 August 2022.

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

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

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.

In your comments to the draft decision you considered that *"Twenty-four months are sufficient to conduct the three mutagenicity studies and skin sensitization studies […]. However, before the OECD 421/422 can be started at least one 14-day range-finding study is needed to allow for proper dose setting. Such a study together with limited examinations requires 4-6 months. For the OECD 421/422 another 18 months are needed for the main study. Thus, for the Annex VIII testing alone, ~24 months would be needed before the OECD 408 (Annex IX) can be started which itself requires another 18 months. As the OECD 414 (Annex IX) in the rat also can only be started after the results of the OECD 421/422 are available […], this study would require 18 months to complete.* [redacted] *would like draw ECHA's attention that based on feedback from two major contract research laboratories (CROs) (*[redacted]*), there is currently a high demand to schedule general toxicology studies […]. Both CROs indicated that it is unlikely they could accommodate the request to complete testing and deliver a final report within 12 or 18 months. Taking into consideration the time required for test substance characterization […] a timeframe of 48 months seems appropriate.".* You did not provide any documentation from a test laboratory to support your request for an additional 12-months extension of the deadline. As explained above, ECHA has in any case already extended the deadline by 12 months. The default deadline will allow sequential testing.

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;

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[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 (https://echa.europa.eu/practical-guides).

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

(2) Information on the Test Material needed in the updated dossier

- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

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).