~~Confidential~~

Helsinki, 24 May 2024

**Addressees**
Registrants of JS_diisopropyl sebacate as listed in Appendix 3 of this decision

**Date of submission of the dossier subject to this decision**
27 March 2013

**Registered substance subject to this decision ("the Substance")**
Substance name: Diisopropyl sebacate
EC/List number: 231-306-4

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

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

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

3. 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).

4. 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 7 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, in rats, to be combined with the screening for reproductive/developmental toxicity requested below.

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

6. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: EU C.1./OECD TG 203)

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

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

8. 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).

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

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.

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. 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.:

- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- *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.)
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

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

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

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

*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 ii., vi., viii., xi., xiv., xv., xvi.

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. Repeated dose toxicity*

24 Test item related repeated dose 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).

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

*0.1.2.1.2. Genotoxicity*

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

*0.1.2.1.3. Toxicity to reproduction or development*

27 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 xi. (reductions in implantation index, delivery index, live birth index and birth index)
- a one generation reproductive toxicity studies with the source substance vi. (litter losses in treated groups, mean litter size reduced)
- a prenatal developmental toxicity study with the source substance/the 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).

*0.1.2.1.4. Assessment outcome*

28 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.

*0.1.2.2. Insufficient data density*

29 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".

30 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.

31 You have provided:

- Repeated dose 28-day oral toxicity study data (OECD TG 407) for three category members (source substances ii., vi. and xvi.);
- Repeated dose 90-day oral toxicity study data (OECD TG 408) for one category member (source substance vi.);
- Bacterial reverse mutation test data (Ames test OECD TG 471) for two category members (source substances xiv., and xv.);
- In vitro cytogenicity data using the in vitro mammalian chromosomal aberration test (OECD TG 473) for two category members (source substances ii. and xi.);
- 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 two category members (source substances vi. and viii.);
- Data for screening for reproductive/developmental toxicity obtained from either a combined repeated dose toxicity study with a reproduction/developmental toxicity screening test (OECD TG 422), a reproduction/developmental toxicity screening test (OECD TG 421), or from an one-generation reproduction toxicity study (OECD TG 415) for three category members (source substances ii., vi., xi.), and
- Prenatal developmental toxicity study data (OECD TG 414) for one category member (source substance vi.).

32 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.*"

33 Information for one category member for skin sensitisation, three for 28-day repeated dose toxicity, one for 90-day toxicity, two for bacterial reverse mutation, two for in vitro cytogenicity, two for in vitro gene mutation, three 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.

34 In your comments to the draft decision, you discuss the data density and you indicate that additional studies that are available on category members could be added as full study reports in a future update of your registration dossier.

35 For identifying any trend, at least two data points must be present because it is impossible to establish whether a property is likely to increase, decrease or stay the same when only one or less data points are available. This allows to identify any changes in the trend. Furthermore, in larger categories there may be breaks in trends which could affect the reliability of interpolation. To confirm that there are no such breakpoints, adequate and reliable information needs to cover also substances within a range of homologous series. (Guidance on IRs and CSA, Section R.6.2.2.2; RAAF on multiconstituent substances and UVCBs)

36 In other words, with increasing number of category members, also the number of data points must increase. For a category of 16 substances, a third and possibly fourth data point are usually necessary to demonstrate consistency of the trend and absence of breaking-points across the category, or to cover specific variations in the chemical structure of some category members.

37 Furthermore, data that is relevant to support the hypothesis should be available for all category members. This could be, e.g.

a. (in vitro) metabolisation data that demonstrates (very) similar hydrolysis rates of all category members, or

b. the information requirements of Annex VIII,

depending on the hypothesis and prediction.

38 Your intended strategy to provide additional studies on category members relies essentially on data which is not yet provided in your dossier; therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

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

39 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.).

40 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.

41 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).

42 For repeated dose toxicity you have provided:

- a sub-acute toxicity study with the source substances ii., vi., xvi.

- a sub-chronic toxicity study with the Substance/source substances vi.

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

44 For mutagenicity you have provided

- *in vitro* gene mutation study in bacteria with the source substances xi. and xiv.
- *in vitro* cytogenicity study with the source substances ii. and xi.
- *in vitro* gene mutation study in mammalian cells with the source substances vi. and viii.

45 No mutagenicity information is available for the Substance or source substances i., ii., iii., iv., v., vii., viii., ix., x., xi., xii., xvi.

46 For reproductive/developmental toxicity you have provided

- a screening for reproductive/developmental toxicity study with the source substances ii., vi., xi.
- a developmental toxicity study with the Substance/source substances vi., xv.

47 No reproductive toxicity information is available for the Substance/source substances i., iii., iv., v., vii., viii., ix., x., xii., xiii., xiv., xvi.

48 Studies of comparable design and duration for the Substance and of the source substances, as listed above, are missing for 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.

49 Furthermore, end-point specific reasons why these studies cannot be considered reliable are explained further below under the requests 1 and 7.

50 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.

51 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)*

52 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.

53 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. Predictions for ecotoxicological properties*

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

55 You predict the properties of the Substance from information obtained from the following source substance(s): category member substances vi., viii., xi.

56 You provide the following reasoning for the prediction of ecotoxicological properties:

- You argue that there are structural similarities between substances of the category.
- You argue that a trend can be observed within the category with regard to physicochemical, environmental fate, and ecotoxicological properties;
- You argue that this trend is related to the carbon chain length of the dicarboxylic acid moiety and of the branching of the alcohol moiety;
- Further, you argue that two category members (source substances i) and ii)) which have relatively higher water solubility (water solubility > 10 mg/L) have ecotoxicological effects, while the remaining category members that have lower water solubility (water solubility < 10 mg/L) do not;
- You report that for the purposes of the aquatic toxicity read-across, you only used the source substance that is the most similar structurally to the Substance (i.e. the target substance).

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

58 "*Based on the experimental data, the majority of category members exhibit no acute and chronic toxicity to aquatic organisms, up to the limit of water solubility. Only two "water soluble" esters of Adipic acid (C6) and short chain alcohols, exhibit ecotoxicolgical effects (CAS 105-99-7, Dibutyl adipate and CAS 6938-94-9, Diisopropyl adipate). Nevertheless, based on the current data, which is considered adequate for an accurate chemical safety assessment of the category, no category member is currently classified for environmental effects according to the 2nd ATP of the Regulation (EC) No.1272/2008 (CLP).*"

59 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance based on an identified trend within the group.

60 We have assessed this information and identified the following issue:

##### *0.1.3.1. Short-term toxicity testing on fish*

###### *0.1.3.1.1. Bias of the prediction from the selection of source substance*

61 In order to make an accurate prediction of (eco)toxicological properties all relevant information must be considered in the prediction. If not all information is considered in the read-across approach, bias can be introduced in the predictions which may result in an over/underestimation in the prediction (RAAF, 2017; Chapter 4.5.1.5.). Bias may be caused by incorrect/incomplete selection of source substance(s); or due to a particular selection of study(ies) performed on the source substance(s).

62 To justify the selection of source substances, you must provide documentation how the source substance(s) have been chosen, for example, what methods/tools have been used to map the field of potential source substance(s), which other substances have been considered and why they have been discarded (RAAF, 2017, Chapter 4.4.1.5/4.5.1.5.). If there are structural analogue(s) not used as source substances and data show significantly different results for the properties to be predicted without any justification for setting aside these different results, then the proposed prediction are considered biased.

63 Your read-across hypothesis is based on an observed trend in increasing aquatic toxicity with

- decreasing carbon chain length (of the dicarboxylic acid moiety and branching of the alcohol moiety) across all category members,
- and increasing water solubility across all category members.

64 In your category justification document, you report that your category approach uses source substances i. – xvi., as listed in Section 0.1.1. above (Scope of the grouping of substances (category)). Further, in your dossier, you report that for the purposes of the aquatic toxicity read-across, you only use the source substance that is the most similar structurally to the Substance (i.e target substance).

65 Specifically, in the present case, you report that source substance xiv. (Dibutyl sebacate, EC 203-672-5, CAS 109-43-3) is used as a source substance for predicting the aquatic toxicity properties of the Substance (i.e., target substance). Source substance xiv. has reported water solubility of <0.05 mg/L. In your dossier, you report that the water solubility of the Substance (i.e. target substance) is 2 mg/L.

66 In addition, as part of your category justification, you report that other source substances used in the category have higher water solubility. Specifically, you report information from the following source substances:

- source substance i. (Diisopropyl adipate, EC 230-072-0, CAS 6938-94-9). Source substance i. has a reported water solubility of 180 mg/L.
- source substance ii. (Dibutyl adipate, EC 203-350-4, CAS 105-99-7). Source substance ii. has a reported water solubility of 35 mg/L.

67 The following study is provided on source substance xiv. showing the following effects:

- study conducted according to ISO 7346/1-3 (Determination of the Acute Lethal Toxicity of Substances to a Freshwater Fish [Brachydanio rerio Hamilton-Buchanan]), (1989).

68 The source study conducted with source substance xiv. showed no effects observed up to the water solubility limit of source substance xiv.

69 The following study is provided on source substance i. showing the following effects:

- source study 1.) OECD TG 203 (2012).

70 Source study 1.) showed an effect concentration well below the solubility limit of source substance i): LC50 (96h, Danio rerio): 37.4 mg/L.

71 The following studies are provided on source substance ii. showing the following effects:

- source study 2.) OECD TG 203 (1985);
- source study 3.) OECD TG 203 (1993).

72 Source study 2.) conducted with with source substance ii) showed an effect concentration well below the solubility limit of source substance ii): LC50 (96h, Pimephales promelas): 3.64 mg/L.

73 Source study 3.) conducted with with source substance ii) showed an effect concentration well below the solubility limit of source substance ii): LC50 (96h, Oryzias latipes): 3.7 mg/L.

74 You have not provided any justification on why you have selected a source substance that has a lower water solubility than that of the Substance (i.e. target substance).

75 As explained above, the water solubility value of the Substance falls between source substances ii) and xiv) and source substances i) and ii) have a higher water solubility than the Substance. Because of their higher water solubility, source substances i) and ii) have a higher bioavailability than the source substance that you have identified (source substance xiv).

76 The available data indicate a trend of increasing aquatic toxicity with increasing water solubility. While ECHA has identified issues with source studies 1.) and 3.) which give rise to the concern that the actual toxicity of source substances i) and ii) may be higher than identified in your registration dossier, they already provide evidence in their present form that indicate the substance exhibits aquatic toxicity below the source substances' respective water solubility limits.

77 However, you have selected a source substance that has a lower water solubility than that of the Substance (i.e. target substance). This means that by using a source substance that has a lower water solubility and consequently a lower bioavailability than that of the Substance (i.e. target substance), your prediction may underestimate the short-term fish toxicity hazard of the Substance.

78 You have not supported and scientifically justified why such such difference in water solubility does not result in differences in the (eco)toxicological properties between the source substance and the Substance (i.e. target substance).

79 Therefore, your predictions are biased and may underestimate the hazards of the Substance.

#### *0.1.3.2. Long-term toxicity testing on aquatic invertebrates*

##### *0.1.3.2.1. Missing robust study summaries*

80 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 include robust study summary for each source study used in the adaptation.

81 In your justification document you have identified the source substances used, but provided only a statement regarding the outcomes of studies conducted with these source substances: "*In none of these tests effects on Daphnia were observed in nominal concentrations well above the limit of water solubility*."

82 You have not provided detailed information on the effect values, methods, results and conclusions, allowing for an independent assessment of the studies. Therefore, you have failed to provide a robust study summary for each source study used in the adaptation as required by Annex XI, Section 1.5.Conclusion

83 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*

84 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. *In vitro* gene mutation study in bacteria

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

### *1.1. Information provided*

86 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 (1994) with the source substance xiv.

(ii) an *in vitro* gene mutation study in bacteria (1985) with the source substance xv.

### *1.2. Assessment of the information provided*

#### *1.2.1. Read-across adaptation rejected*

87 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.

##### *1.2.1.1. Inadequate or unreliable studies on the source substances*

88 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) concurrent strain-specific positive controls, both with and without metabolic activation, are included in each assay and the number of revertant colonies per plate induced by the positive controls demonstrates the effective performance of the assay.

89 In studies (i), and (ii) one of the required strains is not tested:

a) test (i) was performed with the strains *S. typhimurium* TA97, TA98, TA100, TA102 and *E. coli* WP2 uvr A pKM 101 (i.e., the strain TA1535 is missing);

test (ii) was performed with the strains *S. typhimurium* TA 1535, TA 1537, 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);

b) In study (i) concurrent strain-specific positive controls were not included in the study.

90 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.

91 Therefore, the information requirement is not fulfilled.

*1.3. Study design*

92 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**

**2. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study**

93 An *in vitro* mammalian chromosomal aberration study or an *in vitro* mammalian micronucleus study is an information requirement under Annex VIII, Section 8.4.2.

*2.1. Information provided*

94 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 vitro* cytogenicity study in mammalian cells (2004) with the source substance xi.

*2.2. Assessment of the information provided*

*2.2.1. Read-across adaptation rejected*

95 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.

96 Therefore, the information requirement is not fulfilled.

*2.3. Study design*

97 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).

*2.3.1. Assessment of aneugenicity potential*

98 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.

99 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).

## 3. *In vitro* gene mutation study in mammalian cells

100 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.

### *3.1. Triggering of the information requirement*

101 Your dossier contains a read-across adaptation for an *in vitro* gene mutation study in bacteria, and a read-across adaptation for an *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study.

102 The result of the request 1 for information for an *in vitro* gene mutation study in bacteria and of the request 2 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.

103 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.

### *3.2. Information provided*

104 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.

### *3.3. Assessment of the information provided*

#### *3.3.1. Read-across adaptation rejected*

105 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.

106 Therefore, the information requirement is not fulfilled.

### *3.4. Study design*

107 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.

## 4. Short-term repeated dose toxicity (28 days)

108 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.

### *4.1. Information provided*

109 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.

(iii) a sub-acute toxicity study (1986) with the source substance xvi.

*4.2. Assessment of the information provided*

*4.2.1. Read-across adaptation rejected*

110 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.

111 Therefore, the information requirement is not fulfilled.

*4.3. Study design*

112 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.).

113 The study design is addressed in request 5.3

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

114 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 7.).

115 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.

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

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

## 5. Screening study for reproductive/developmental toxicity

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

*5.1. Information provided*

119 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 studies (1988) with the source substance vi.;

(iii) a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (2003) with the source substance xi.

*5.2. Assessment of the information provided*

*5.2.1. Read-across adaptation rejected*

120 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.

121 Therefore, the information requirement is not fulfilled.

*5.3. Study design*

122 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.

123 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).

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

125 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.

126 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.).

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

128 The information requirement for the 28-day repeated dose toxicity study is not fulfilled for the reasons explained under request 4.

## 6. Short-term toxicity testing on fish

129 Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

*6.1. Information provided*

130 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 short-term toxicity study on fish (1989) with the source substance xiv., as listed in Section 0.1.1. above (dibutyl sebacate, EC 203-672-5)

*6.2. Assessment of the information provided*

*6.2.1. Read-across adaptation rejected*

131 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.

132 Therefore, the information requirement is not fulfilled.

133 In your comments to the draft decision, you mention the adaptation possibility of performing the long-term toxicity to fish study (OECD TG 210; see request 10) instead of performing a new OECD TG 203 study as requested.

134 Annex VIII, Section 9.1.3, Column 2 specifies that the short-term toxicity study does not need to be conducted if a long-term aquatic toxicity study on fish is available.

135 At present no long-term toxicity study on fish is provided in the IUCLID dossier, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

**Reasons related to the information under Annex IX of REACH**

## 7. Sub-chronic toxicity study (90 days)

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

### *7.1. Information provided*

137 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.

### *7.2. Assessment of the information provided*

#### *7.2.1. Read-across adaptation rejected*

138 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.

##### *7.2.1.1. Inadequate or unreliable studies on the source substance(s)*

139 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.

140 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 of organs for which the pathological examination was perfomed is missing

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

141 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 in paragraphs 47-49 of OECD TG 408

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

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

143 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.

*7.3. Study design*

144 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.

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

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

## 8. Pre-natal developmental toxicity study in one species

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

*8.1. Information provided*

148 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.

*8.2. Assessment of the information provided*

*8.2.1. Read-across adaptation rejected*

149 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.

150 Therefore, the information requirement is not fulfilled.

*8.3. Study design*

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

152 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).

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

## 9. Long-term toxicity testing on aquatic invertebrates

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

### *9.1. Information provided*

155 You have adapted this information requirement and provided the following justification:

(i) You claim that short-term aquatic toxicity test showed no effects for the Substance.

(ii) You mention that the Substance is readily biodegradable and has a high potential for adsorption. On this basis, you claim that releases to surface waters are negligible and chronic exposure of aquatic organisms is unlikely.

(iii) You refer to the PFAE linear category and mention that members of the category are not bioaccumulative.

(iv) You mention that "*Adverse effects on aquatic organisms were observed for Adipic acid ester of the PFAE linear category with short chain alcohols exclusively and are not expected or observed for Sebacic acid ester of the PFAE linear category.*"

(v) You mention animal welfare.

### *9.2. Assessment of the information provided*

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

157 Short-term aquatic invertebrate studies (in this case, OECD TG 202 studies) cover different investigations than the ones that are needed to fulfil the long-term aquatic invertebrate toxicity information requirement (in this case, the investigations of OECD TG 211).

158 Because of this reason, the finding that shows a lack of toxicity for a 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.

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

#### *9.2.1. Your justification to omit the study has no legal basis*

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

161 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 aquatic invertebrates under Column 1.

162 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.

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

164 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.

165 Regarding your justification under point (v), we have identified the following issue.

*9.2.1. Your justification regarding minimisation of animal testing is rejected*

166 Minimisation of 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.

*9.3. Conclusion*

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

168 Therefore, the information requirement is not fulfilled.

## 10. Long-term toxicity testing on fish

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

*10.1. Information provided*

170 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 (EC 203-350-4, CAS 105-99-7, Dibutyl adipate and EC 230-072-0, CAS 6938-94-9, Diisopropyl adipate). 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*

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

172 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).

173 Because of this reason, the finding that shows a lack of toxicity for a 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.

174 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.

175 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*

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

177 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.

178 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.

*10.2.2. Your justification regarding minimisation of vertebrate testing is rejected*

179 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.

*10.2.3. Conclusion*

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

181 Therefore, the information requirement is not fulfilled.

*10.3. Study design*

182 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.).

## 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 and did not amend 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 indicate that *"We are also aware of several other draft compliance checks that have been received for similar substances. Several of these substances are managed by our consortium, and if confirmed we will aim at performing the required studies in an optimized way. Hence, studies would be performed in the same laboratory […]. However, we will be limited then by the number of studies that can be performed by the laboratory, as all studies will not run in parallel. Therefore, in order to be able to optimized the performance of the studies and not be limited by the capacity of the laboratory, we propose to extend the deadline for submiting the studies through an updated dossier to 'exact date – 48 months from the date of the decision'."* You did not provide any justification from a test laboratory to support your request for an additional 12-months extension of the deadline. As explained above, ECHA has already extended the deadline by 12 months. Therefore in the absence of relevant documentation justifying your request for additional extension ECHA cannot extend the deadline further.

After further assessment of the information included in your dossier on skin sensitisation, the information provided is considered compliant and therefore the original request for this standard information requirement has been removed from this decision.

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] |

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

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

- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include all constituents of each Test Material and their concentration values.

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).