~~Confidential~~

Helsinki, 24 May 2024

Addressees
Registrants of Diisopropyl adipate as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
02 May 2013

Registered substance subject to this decision ("the Substance")
Substance name: Diisopropyl adipate
EC/List number: 230-072-0

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. Surface tension (Annex VII, Section 7.6.; test method: EU A.5./OECD TG 115)

2. 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);

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

4. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202)

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

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

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

7. 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: 8. In vitro gene

mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

8. Justification for an adaptation of the short-term repeated dose toxicity study (28 days) (Annex VIII, Section 8.6.1., Column 2) based on the request 11 below, or in case the sub-chronic toxicity study (90 days) is not requested:

   Short-term repeated dose toxicity (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

9. 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

10. 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

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

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

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

14. 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)

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)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study on aquatic plants (Annex VII, Section 9.1.2.)
- *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 ii. and vi.

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 substances cause the same type of effects.

23 You predict no hazardous effects for the category substances but the study results related to repeated dose toxicity, mutagenicity, and reproductive/ developmental toxicity obtained with the source substances 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 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.

0.1.2.1.2. Genotoxicity

26 Positive results for mutagenicity are observed in the *in vitro* mammalian cell gene mutation study conducted with the source substance vi.

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 substance ii. (reduction of pup viability)
- a one generation reproductive toxicity study 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 effects. 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:

- Skin sensitisation data obtained from a guinea pig maximisation test (OECD TG 406) for one category member (source substance ii.);
- 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.);
- Bacterial reverse mutation test (Ames test, OECD TG 471) for one category member (source substance ii.);
- *In vitro* cytogenicity data using the *in vitro* mammalian chromosomal aberration test (OECD TG 473) for one category member (source substances ii.);
- *In vivo* mammalian cell gene mutation data obtained from a mammalian erythrocyte micronucleus test (OECD TG 474) for one category members (source substances ii.);
- 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., vi.), 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, one for 28-day repeated dose toxicity, one for 90-day toxicity, one for bacterial reverse mutation test, one for in vitro cytogenicity, one for in vivo mammalian cell gene mutation, 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)

34 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.).

35 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.

36 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).

37 For skin sensitisation you have provided:

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

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

39 For repeated dose toxicity you have provided:

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

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

41 For mutagenicity you have provided

- *in vitro* gene mutation study in bacteria with the source substance ii.
- *in vitro* cytogenicity study with the source substance ii.
- *In vivo* gene mutation study with the source substance ii

42 No mutagenicity information is available for the Substance or for the source substances iii., iv., v., vi., vii., viii., ix., x., xi., xii., xiii., xiv., xv. and xvi.

43 For reproductive/developmental toxicity you have provided

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

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

45 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.

46 Furthermore, end-point specific reasons why these studies cannot be considered reliable are explained further below under the request 11.

47 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.

0.1.2.4. Inadequate or unreliable studies on the source substances

48 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.

49 Specific reasons why the studies on the source substances do not meet these criteria are explained further below under the applicable information requirement sections 11. Therefore, no reliable predictions can be made for these information requirements.

0.1.3. Predictions for ecotoxicological properties

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

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

52 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).

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

54 "*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)*."

55 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.

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

0.1.3.1. Short-term aquatic toxicity

0.1.3.1.1. Read-across prediction may underestimate hazard

57 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.).

58 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 substance(s). An explanation why such differences do not affect the read-across hypothesis must to be provided and supported by scientific evidence.

59 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.

60 In your category justification document, you report that the water solubility of source substance ii. is 35 mg/L and the water solubility of the Substance (i.e. target substance) is 180 mg/L.

61 The available data on short-term toxicity testing on fish and aquatic invertebrates indicate that effect concentrations below their respective water solubility limit were observed for water soluble category members:

- source substance ii) (molecular formula: $C_{14}H_{26}O_4$; water solubility: 35 mg/L);
- the Substance (molecular formula: $C_{12}H_{22}O_4$; water solubility: 180 mg/L).

62 While for poorly water soluble substances (WS < 1 mg/L), no effects were observed up to their respective water solubility limit, e.g.:

- source substance vi. (molecular formula: $C_{22}H_{42}O_4$; water solubility: 0.78 mg/L);
- source substance xi. (molecular formula: $C_{25}H_{48}O_4$; water solubility: <4.0E-4 mg/L);
- source substance xv. (molecular formula: $C_{26}H_{50}O_4$; water solubility: <1 mg/L).

63 While ECHA has identified issues with studies conducted with the Substance and source substance ii., which give rise to the concern that their actual toxicity may be higher than identified in your registration dossier, they already provide evidence in their present form that indicate these substances exhibit aquatic toxicity below their limit of water solubility. Further, the available data indicate an overall trend of increasing aquatic toxicity with decreasing carbon chain length and increasing water solubility.

64 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, your prediction may underestimate the short-term aquatic toxicity hazard of the Substance. You have not supported and scientifically justified why such such difference in water solubility does not result in differences in the ecotoxicological properties between the source substance and the Substance.

0.1.3.1.2. Inadequate or unreliable studies on the source substances

65 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.

66 Specific reasons why the studies on the source substance do not meet these criteria are explained further below under the applicable information requirement sections 4, 5, and 10. Therefore, no reliable predictions can be made for these information requirements.

0.1.4. Conclusion

67 In your comments to the draft decision, you explain that this substance has been registered as being part of the [redacted], under the Category approach used for [redacted], where you planned to follow the [redacted] subcategory strategy to fulfill the endpoints.

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

69 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

70 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. Surface tension

71 Surface tension of an aqueous solution is an information requirement under Annex VII to REACH (Column 1 of Section 7.6).

1.1. Information provided

72 You have adapted this information requirement by using Column 2 of Annex VII, Section 7.6. To support the adaptation, you have provided the following information:

- *"In accordance with Regulation (EC) No 1907/2006, Column 2 of Annex VII, Section 7.6, the study does not need to be conducted because based on structure, surface activity is not expected and no surface activity can be predicted and surface activity is not a desired property of the material."*

1.2. Assessment of the information provided

73 Under Annex VII, Section 7.6, Column 2, first indent, the study needs to be conducted if based on structure of the substance, surface activity is expected or can be predicted.

74 You claim that based on structure, surface activity is not expected and no surface activity can be predicted and surface activity is not a desired property of the material.

75 However, based on the structure of the Substance, surface activity can be expected, because the Substance has hydrophilic (ester) and lipophilic (alkyl chain) moieties.

76 Further, in section 3.5 of your registration dossier, you report that the Substance is used in Product Category 35 (PC 35: Washing and cleaning products). Further, you report technical functions of the Substance in its industrial uses, including

- "Industrial use of Laundry products Laundry aid (gasing)";
- "Brushing and industrial cleaning solution";
- "Industrial use of Metal Treatment Products* Metal cleaner (degreaser, descaler, etch)"
- "Industrial use of Food beverage and pharmacos products Process cleaner; Cleaning In place (CIP) process"
- "Industrial use of Food beverage and pharmacos products Process cleaner";
- "Industrial use of Vehicle cleaning Products Train cleaner".

77 The reported PC 35 uses indicate that surface activity may be a desired property of the substance.

78 Therefore, your adaptation is rejected.

2. Skin sensitisation

79 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).

2.1. 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 the following experimental data from the source substances:

(i) a Guinea Pig Maximisation Study (1989) with the source substance ii.

2.2. Assessment of the information provided

2.2.1. 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.

2.3. Study design

83 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.

84 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.

3. 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.

3.1. 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 substance:

(i) an *in vitro* gene mutation study in bacteria (1996) with the source substance ii.

3.2. Assessment of the information provided

3.2.1. 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.

88 Therefore, the information requirement is not fulfilled.

3.3. Study design

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

4. Short-term toxicity testing on aquatic invertebrates

90 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

4.1. Information provided

91 You have provided:

(i) Short-term toxicity study on Daphnia magna (1993) with the source substance ii., as listed in section 0.1 of this Decision;

(ii) Short-term toxicity study on Daphnia magna (2012) with the Substance.

92 In addition, you have adapted this information requirement by using column 1 of Annex VII, Section 9.1.1., and provided the following information:

(iii) "*In accordance to Regulation (EC) No. 1907/2006, column 2 of Annex VII chapter 9.1, a study on the acute toxicity to invertebrates does not need to be conducted if a long term aquatic toxicity study on invertebrates is available*."

4.2. Assessment of the information provided

4.2.1. The provided studies do not meet the specifications of the test guideline

93 To fulfil the information requirement, a study must comply with OECD TG 202 (Article 13(3) of REACH). Therefore, the following specification(s) must be met:

Technical specifications impacting the sensitivity/reliability of the test

a) the test duration is 48 hours or longer;

Characterisation of exposure

b) analytical monitoring must be conducted. A reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;

Reporting of the methodology and results

c) the test design is reported (*e.g.* static or semi-static test, number of replicates);
d) the number of immobilised daphnids is determined at 24 and 48 hours. Data are summarised in tabular form, showing for each treatment group and control, the number of daphnids used, and immobilisation at each observation.

94 In study (i):

Technical specifications impacting the sensitivity/reliability of the test

a) the test duration was 24 hours;

Characterisation of exposure

b) no analytical monitoring of exposure was conducted.

95 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, you used an exposure duration that is shorter than the requirement of the TG. The resulting effect concentration may be higher than the effect concentration that would have been measured in a test with a 48-hour exposure duration. Further, you have not measured the exposure concentration

of the test substance in any of the treatment groups. Because of this, ECHA cannot independently verify if the concentration of the test substance remained stable throughout the exposure duration of the test.

96 On this basis, the specification(s) of OECD TG 202 are not met.

97 In study (ii):

Characterisation of exposure

b) no analytical monitoring of exposure was conducted

Reporting of the methodology and results

c) on the test design, you have not specified what nominal concentrations were tested and the number of replicates for each concentration tested in the treatment groups;
d) tabulated data on the number of immobilised daphnids after 24 and 48 hours for each treatment group and control are not reported.

98 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, you have not measured the exposure concentration of the test substance in any of the treatment groups. Because of this, ECHA cannot independently verify if the concentration of the test substance remained stable throughout the exposure duration of the test.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, you have not reported key pieces of information (including the number of immobilised daphnids after 24 and 48 hours in the control) that are relevant to the validity criteria of the study. Because of this, ECHA cannot independently verify the validity of study (ii).

99 On this basis, the specification(s) of OECD TG 202 are not met.

4.2.1. Study not conducted according to GLP

100 (Eco)toxicological studies must comply with GLP or another recognised international standard; Article 13(4) of REACH.

101 You have indicated that study (i) and (ii) are "not GLP-compliant", without further explanation.

102 The tests do not comply with GLP or another recognised international standard and are therefore rejected.

4.2.2. Read-across adaptation rejected

103 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.

4.2.3. Your justification to omit the study is rejected

104 ECHA understands that in the provided information under point (iii), you reference column 1 of Annex VII, Section 9.1.1., by stating that "*a study on the acute toxicity to invertebrates does not need to be conducted if a long term aquatic toxicity study on invertebrates is available*".

105 However, as explained under request 13 of this Decision, your registration dossier currently does not include a long-term aquatic toxicity study on invertebrates.

4.3. Conclusion

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

107 Therefore, the information requirement is not fulfilled.

5. Growth inhibition study aquatic plants

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

5.1. Information provided

109 You have provided:

(i) Growth inhibition study on algae (2012) with the Substance.

110 In addition, 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:

(ii) Growth inhibition study on algae (1993) with the source substance ii., as listed in section 0.1 of this Decision;

5.2. Assessment of the information provided

5.2.1. The provided studies do not meet the specifications of the test guideline

111 To fulfil the information requirement, a study must comply with OECD TG 201 (Article 13(3) of REACH). Therefore, the following specifications must be met:

112 Technical specifications impacting the sensitivity/reliability of the test

a) the pH of the control medium does not increase by > 1.5 units;

b) if a solvent is used, its concentration is ≤ 100 µg/L;

113 Characterisation of exposure

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

114 Reporting of the methodology and results

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

115 In study (i):

116 Characterisation of exposure

c) no analytical monitoring of exposure was conducted;

117 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, you have not measured the exposure concentration of the test substance in any of the treatment groups. Because of this, ECHA cannot independently verify if the concentration of the test substance remained stable throughout the exposure duration of the test.

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

119 In study (ii):

120 Technical specifications impacting the sensitivity/reliability of the test

a) the pH increase in the controls was 2.8 units;

b) the concentration of solvent present in the test solutions was 100 mg/L;

121 Characterisation of exposure

c) no analytical monitoring of exposure was conducted;

122 Reporting of the methodology and results

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

123 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, you have not measured the exposure concentration of the test substance in any of the treatment groups. Because of this, ECHA cannot independently verify if the concentration of the test substance remained stable throughout the exposure duration of the test. In addition to this, the pH increase observed in the test may have affected the growth rate observed in the control and may have impacted the difference observed between the control and treatment groups.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, you have not reported key pieces of information (e.g. algal biomass for each treatment group and control determined in each flask at least daily) that are relevant to the validity of the study. Because of this, ECHA cannot independently verify if study (ii) is valid.

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

5.2.2. Study not conducted according to GLP

125 (Eco)toxicological studies must comply with GLP or another recognised international standard; Article 13(4) of REACH.

126 You have indicated that study (i) is "not GLP-compliant", without further explanation.

127 The test does not comply with GLP or another recognised international standard and is therefore rejected.

5.2.3. Read-across adaptation rejected

128 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.

Reasons related to the information under Annex VIII of REACH

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

129 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.

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) 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.

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.

6.1. Study design

133 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).

6.1.1. Assessment of aneugenicity potential

134 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.

135 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).

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

136 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.

7.1. Triggering of the information requirement

137 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.

138 The information for the *in vitro* gene mutation study in bacteria and for the *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study provided in the dossier are rejected for the reasons provided in requests 3 and 6.

139 The result of the requests for an *in vitro* gene mutation study in bacteria and 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.

140 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.

7.1. Information provided

141 You have not provided data for *in vitro* gene mutation study in mammalian cells but instead you have included a data waiver for an *in vivo* mammalian gene mutation study:

(i) Waiver justification: *"Testing according to OECD TG 476 is still ongoing. The dossier will be updated as soon as possible and the Chemical Safety Assessment according to Annex I of Regulation (EC) No 1907/2006 will be re-evaluated based on the outcome of this new study."*

7.2. Assessment of the information provided

7.2.1. Waiver justification rejected

142 No information on the Substance is available for the information requirement and there is no basis for waiver justification (i) either.

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

7.3. Study design

144 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.

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

145 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.

8.1. Information provided

146 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.

8.2. Assessment of the information provided

8.2.1. Read-across adaptation rejected

147 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.

148 Therefore, the information requirement is not fulfilled.

8.3. Study design

149 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.).

150 The study design is addressed in request 9.3.

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

151 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 11.3).

152 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.

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

154 Therefore, you are requested to either submit:

- a justification for the adaptation according to Annex VIII, Section 8.6.1., Column 2, based on request 11.3; or
- a 28-day study as per the study design described in 9.3. in case the 90-day study is not requested in the adopted decision.

9. Screening study for reproductive/developmental toxicity

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

9.1. Information provided

156 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.

9.2. Assessment of the information provided

9.2.1. Read-across adaptation rejected

157 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.

158 Therefore, the information requirement is not fulfilled.

9.3. Study design

159 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.

160 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).

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

162 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.

163 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.).

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

165 The information requirement for the 28-day repeated dose toxicity study is not fulfilled for the reasons explained under request 8.3.

10. Short-term toxicity testing on fish

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

10.1. Information provided

167 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 (1985) with the source substance ii., as listed in Section 0.1. of this Decision;

(ii) a short-term toxicity study on fish (1993) with the source substance ii., as listed in Section 0.1. of this Decision;

(iii) a short-term toxicity study on fish (2012) with the Substance.

10.2. Assessment of the information provided

10.2.1. The provided studies do not meet the specifications of the test guideline

168 To fulfil the information requirement, a study must comply with OECD TG 203 (Article 13(3) of REACH). Therefore, the following specification(s) must be met:

169 Technical specifications impacting the sensitivity/reliability of the test

a) although not generally recommended, if a solvent is used, its concentration in the test water is below its critical micelle concentration (if relevant) and, in all case, ≤ 100 mg/L (or 0.1 mL/L);
b) at least 5 concentrations are tested;

170 Characterisation of exposure

c) analytical monitoring must be conducted. A reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available.

171 In study (ii):

172 Technical specifications impacting the sensitivity/reliability of the test

a) the concentration in solvent present in the test solutions was 200 mg/L;

173 Characterisation of exposure

c) no analytical monitoring of exposure was conducted;

174 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically you have used a higher solvent concentration that what is recommended in the TG. Further, you have not measured the exposure concentration of the test substance in any of the treatment groups. Because of this, ECHA cannot independently verify if the concentration of the test substance remained stable throughout the exposure duration of the test.

175 On this basis, the specification(s) of OECD TG 203 are not met.

176 In study (iii):

177 Technical specifications impacting the sensitivity/reliability of the test

b) only 4 concentrations were tested;

178 Characterisation of exposure

c) no analytical monitoring of exposure was conducted.

179 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically the number of concentrations tested may have effected the measured effect concentration value. In addition to this, you have not

measured the exposure concentration of the test substance in any of the treatment groups. Because of this, ECHA cannot independently verify if the concentration of the test substance remained stable throughout the exposure duration of the test.

180 On this basis, the specification(s) of OECD TG 203 are not met.

10.2.1. Study not conducted according to GLP

181 (Eco)toxicological studies must comply with GLP or another recognised international standard; Article 13(4) of REACH.

182 You have indicated that study (iii) is "not GLP-compliant", without further explanation.

183 The test does not comply with GLP or another recognised international standard and is therefore rejected.

10.2.2. Read-across adaptation rejected

184 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.

10.3. Conclusion

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

186 Therefore, the information requirement is not fulfilled.

Reasons related to the information under Annex IX of REACH

11. Sub-chronic toxicity study (90-day)

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

11.1. Information provided

188 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 study (TG 415) (1988) with the source substance vi.

11.2. Assessment of the information provided

11.2.1. Read-across adaptation rejected

189 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.

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

190 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.

191 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 histopathological examination was perfomed is missing.

192 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 and ovary 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.

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

194 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.

11.3. Study design

195 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.

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

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

12. Pre-natal developmental toxicity study in one species

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

12.1. Information provided

199 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.

12.2. Assessment of the information provided

12.2.1. Read-across adaptation rejected

200 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.

201 Therefore, the information requirement is not fulfilled.

12.3. Study design

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

203 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).

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

13. Long-term toxicity testing on aquatic invertebrates

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

13.1. Information provided

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

(i) You claim that the Substance is rapidly biodegrading and on this basis, you claim that exposure of aquatic organisms is unlikely

(ii) You claim that "*a test according to OECD 211 is currently ongoing. The dossier will be updated as soon as possible and the Chemical Safety Assessment according to Annex I of Regulation (EC) No 1907/2006 will be re-evaluated based on the outcome of this new study*."

13.2. Assessment of the information provided

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

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

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

209 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 invertebrates under Column 1.

210 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.

211 Regarding your justification under point (ii), we have identified the following issue.

13.2.2. Your claim regarding an ongoing test with the Substance is unsubstantiated

212 No information on the Substance is available for the information requirement and there is no basis for waiver justification (i) either. Further, we note that no testing proposal has been submitted to ECHA for the Substance and that the current version of the registration dossier was submitted in 2013.

13.3. Conclusion

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

214 Therefore, the information requirement is not fulfilled.

14. Long-term toxicity testing on fish

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

14.1. Information provided

216 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 substances i. and ii., as listed in 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.

14.2. Assessment of information provided

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

218 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).

219 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.

220 Further, ECHA notes, that under point (i) in your justification, you mention the Substance as one of the two category members that did show toxicity in short-term aquatic toxicity studies.

221 Finally, 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.

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

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

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

224 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.

225 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.

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

14.2.2. Your justification regarding minimisation of vertebrate testing is rejected

227 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.

14.3. Conclusion

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

229 Therefore, the information requirement is not fulfilled.

14.4. Study design

230 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 request(s) 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 *"36 months seems not to be enough time to complete all these studies considering CRO's schedules and planning. CRO will provide the schedule shortly."* You did not provide any justification from a test laboratory to support your request for extending the deadline from 36 months to an indeterminate longer period of time. As explained above, ECHA has already extended the deadline by 12 months.

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]

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).