~~Confidential~~

Helsinki, 20 September 2023

Addressee(s)
Registrant(s) of JS_Dimethyl_Adipate as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
26/10/2021

Registered substance subject to this decision ("the Substance")
Substance name: Dimethyl adipate
EC/List number: 211-020-6

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 ***4 January 2027***.

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

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

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

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

2. Only if a negative result in Annex VII, Section 8.4.1. 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)

3. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: OECD TG 421 or 422)

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

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

5. 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)

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

7. 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. Read-across adaptation rejected

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

- *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Screening for reproductive/developmental toxicity, (Annex VIII, Section 8.7.1.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

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. Scope of the grouping of substances (category)

5 You provide a read-across justification document in IUCLID Section 13.2.

6 For the purpose of this decision, the following abbreviations are used for the category members:

- Reaction mass of dimethyl adipate, dimethyl glutarate and dimethyl succinate, EC 906-170-0 (source substance 1), DBE;
- Dimethyl glutarate, EC 214-277-2 (source substance 2);
- Dibutyl adipate, EC 203-350-4 (source substance 3).

7 You justify the grouping of the substances as: "The similarities in molecular structures, properties, functions and uses of the dibasic esters enables read-across of the available data to fulfil specific information requirements under REACH. Therefore, it is expected that the substances share similar physico-chemical properties, as well as properties regarding environmental fate, environmental toxicology, and mammalian toxicology. The available data support this hypothesis and underpin the read-across between the substances" […] "The toxicity of each of these substances is similar...".

8 You define the applicability domain as: "All category members are dicarboxylic acid esters".

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

0.1.1. Incomplete description of the applicability domain of the category

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

11 Your definition of the applicability domain of the category can be summarised as: "all category members are dicarboxylic acid esters".

12 Your read-across justification document contains no information on the inclusion or exclusion criteria from the category: e.g. the type of alcohol (e.g. methanol, butanol or isobutanol) and dicarboxylic acids, the alkyl chain branching and length of the constituents of the category members.

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

0.2. Predictions for toxicological properties

14 You provide a read-across justification document in IUCLID Section 13.2.

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

- Reaction mass of dimethyl adipate, dimethyl glutarate and dimethyl succinate, EC 906-170-0 (source substance 1), DBE;
- Dimethyl glutarate, EC 214-277-2 (source substance 2);
- Dibutyl adipate, EC 203-350-4 (source substance 3).

16 You provide the following reasoning for the prediction of toxicological properties: "The similarities in molecular structures, properties, functions and uses of the dibasic esters enables read-across of the available data to fulfil specific information requirements under REACH. Therefore, it is expected that the substances share similar physico-chemical properties, as well as properties regarding environmental fate, environmental toxicology, and mammalian toxicology", and "The justification for read across for the human health toxicity endpoints is that the esters in all compounds are expected to be readily hydrolysed by the carboxylesterases present throughout the body. Following the metabolism of these esters the toxicity will be dependant on the acids and alcohols released. There are sufficient toxicological information on the esters, acids and alcohols to characterise the hazards of the category members."

17 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effect. You predict the properties of your Substance to be quantitatively equal to those of the source substance based on an identified trend within the group.

18 We have identified the following issue(s) with the prediction(s) of toxicological properties:

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

19 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.).

20 Supporting information must include bridging studies to compare properties of the category members.

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

22 You provided several studies on source substances, including two in vitro gene mutation studies in bacteria and one on mammalian cells, a sub-chronic study and two pre-natal developmental toxicity studies. You provided one sub-chronic study on the target substance, but none that are relevant to the adapted information requirements with e.g. shorter exposure duration (bridging studies). Specific reasons why this study cannot be considered reliable are explained further below under the relevant information requirement in section 3. Thus the data set reported in the technical dossier does not include relevant, reliable and adequate information for the source substance(s) to support your read-across hypothesis.

23 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.

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

24 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.

25 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 1, 3, 4 and 5. Therefore, no reliable predictions can be made for these information requirements.

26 In your comments to the draft decision, you submitted a new read across justification document. In that document you present a strategy relying on the generation of additional supporting information on the Substance and on the analogue substances ECs 906-170-0, 907-870-9, 936-196-8, 214-277-2 and 203-419-9, 203-350-4. ECHA acknowledges your intention. As indicated in your comments, this strategy relies essentially on data, which is yet to be generated, therefore no conclusion on the compliance can currently be made.

0.3. Conclusion on the read-across approach

27 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.

Reasons related to the information under Annex VII of REACH

1. *In vitro* gene mutation study in bacteria

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

1.1. Information provided

29 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 (1988) with the source substance Reaction mass of dimethyl adipate and dimethyl glutarate and dimethyl succinate, EC 906-170-0, DBE;

(ii) an *in vitro* gene mutation study in bacteria (2000) with the source substance dibutyl adipate, EC 203-350-4;

(iii) an *in vitro* gene mutation study in bacteria (1980) with the source substance Reaction mass of dimethyl adipate and dimethyl glutarate and dimethyl succinate, EC 906-170-0, DBE.

1.2. Assessment of the information provided

1.2.1. Read-across adaptation rejected

30 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 substance(s)

31 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:

i. 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);

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

32 In study (i):

a) the test was performed with the strains TA98 and TA100 (i.e., the 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) strain(s) are missing);

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

33 In study (iii):

c) the test was performed with the TA1535, TA1537, TA98, TA100 strains (i.e., one strain which is either S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101) strain(s) is missing);

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

34 Therefore, the studies (i) and (iii) submitted in your adaptation, as currently reported in your dossier, do not provide an adequate and reliable coverage of the key parameter(s) required by the OECD TG 471.

35 Therefore, the information requirement is not fulfilled.

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

1.3. Specification of the study design

37 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* gene mutation study in mammalian cells

38 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.

2.1. Triggering of the information requirement

39 Your dossier contains (I) a negative result for in vivo micronucleus study, and (II) inadequate data for *in vitro* gene mutation study in bacteria.

40 The in vitro gene mutation study in bacteria provided in the dossier is rejected for the reasons provided in Section 0.1.

41 The result of the request 1 will determine whether the present requirement for an in vitro mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3. is triggered.

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

2.2. Information provided

43 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 (2002) with the source substance dimethyl glutarate, EC 214-277-2.

2.3. Assessment of the information provided

2.3.1. Read-across adaptation rejected

44 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.

45 Therefore, the information requirement is not fulfilled.

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

2.4. Specification of the study design

47 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.

3. Screening study for reproductive/developmental toxicity

48 A screening for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1., if there is no evidence from

analogue substances, QSAR or in vitro methods that the substance may be a developmental toxicant.

3.1. Information provided

49 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 study similar to a one-generation reproductive toxicity study (OECD TG 415) with the source substance Reaction mass of dimethyl adipate, dimethyl glutarate and dimethyl succinate, EC 906-170-0.

3.2. Assessment of the information provided

3.2.1. Read-across adaptation rejected

50 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 above.

3.2.2. Source study not adequate for the information requirement

51 Under Annex XI, Section 1.5., the study to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case EU B.63/OECD TG 421 or EU B.64/OECD TG 422. Therefore, the following specifications must be met:

a) the highest dose level aims to induce toxicity or aims to reach the limit dose;
b) the exposure duration is at least four weeks for males, including a minimum of two weeks prior to mating, and approximately 63 days for females to cover premating, conception, pregnancy and at least 13 days of lactation;
c) thyroid hormone levels are measured;
d) offspring parameters such as anogenital distance.

52 In study (i):

a) the highest dose levels tested was 1 mg/L (i.e., below the limit dose of the OECD TG 421/422) and no adverse effect were observed and no justification for the dose setting was provided;
b) the exposure duration did not include gestation days 19 to post partum day 3 for females and is therefore incomplete;
c) thyroid hormone levels were not measured;
d) data on anogenital distance is missing.

53 The information provided does not provide an adequate and reliable coverage of the specifications required by the OECD TG 421/422.

54 Based on the above, the study is/studies are not an adequate basis for your read-across predictions.

55 Therefore, the information requirement is not fulfilled.

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

3.3. Specification of the study design

57 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.

58 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).

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

Reasons related to the information under Annex IX of REACH

4. Sub-chronic toxicity study (90 days)

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

4.1. Information provided

61 You have provided:

(i) a sub-chronic toxicity study (2000) with the Substance.

62 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) a sub-chronic toxicity study (1987) with the source substance Reaction mass of dimethyl adipate, dimethyl glutarate and dimethyl succinate, EC 906-170-0; DBE.

4.2. Assessment of the information provided

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

63 To fulfil the information requirement or, in the case of a source study, to provide adequate and reliable coverage of key parameters of a study, the sub-chronic toxicity study (90 days) has to meet the requirements of the OECD TG 408/413. Therefore, the following specifications must be met:

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

b) the highest dose level aims to induce toxicity or reach the limit dose.

64 In study (i):

a) there was only one dose level.

65 In study (i) and (ii):

b) you do not provide any justification for the dose setting while the highest dose level tested was 400 mg/m^3, which is below the limit dose of the test guideline, and no adverse effects were observed.

66 The information provided does not cover the specification(s) required by the OECD TG 408/413.

4.2.2. Read-across adaptation rejected

67 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 above.

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

69 Therefore, the information requirement is not fulfilled.

70 In your comments to the draft decision, you submitted a new read across justification document. In that document you present a strategy relying on the generation of additional supporting information on the Substance and on the analogue substances ECs 906-170-0, 907-870-9, 936-196-8, 214-277-2 and 203-419-9. ECHA acknowledges your intention. As indicated in your comments, this strategy relies essentially on data, which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

4.3. Specification of the study design

71 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. Even though the information indicates that human exposure to the Substance by the inhalation route is likely, there is no concern for severe local effects following inhalation exposure. Furthermore, ECHA points out that no repeated dose toxicity study by the oral route is available. Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

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

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

5. Pre-natal developmental toxicity study in one species

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

5.1. Information provided

75 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 (similar to OECD 414) in rats (1995) with the source substance Reaction mass of dimethyl adipate, dimethyl glutarate and dimethyl succinate, EC 906-170-0, DBE;

(ii) a pre-natal developmental toxicity study (EPA OPPTS 870.3700) in rabbits (1998) with the source substance dimethyl glutarate, EC 214-277-2.

5.2. Assessment of the information provided

5.2.1. Read-across adaptation rejected

76 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.

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

77 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall be normally performed for a particular information requirement, in this case OECD TG 414. Therefore, the following specifications must be met:

a) the highest dose level aims to induce toxicity or aims to reach the limit dose;

b) the test chemical is administered via oral gavage and justification should be provided for other routes;

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

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

78 In study (i):

a) the highest dose levels tested was 1 mg/L, which is below the limit dose of the test guideline, and no adverse effect were observed (i.e. the trend for maternal body weight is not clear: "Body weight changes in maternal rats exposed to either 0.4 or 1.0 mg/L, were reduced, whereas those from the 0.16 mg/L were not"), and no justification for the dose setting;

c) data on the examination of the dams, including incidence and severity, are missing; In particular, the following investigations are missing: thyroid gland/thyroid hormone measurements;

d) data on the examination of the foetuses, including incidence and severity, are missing; In particular, the following investigations are missing: fetus anogenital distance.

79 In studies (i) and (ii):

b) the substance was administered via inhalation route without justification.

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

81 Therefore, the information requirement is not fulfilled.

82 In your comments to the draft decision, you submitted a new read across justification document. In that document you present a strategy relying on the generation of additional supporting information on the Substance and on the analogue substances ECs ECs 906-170-0, 907-870-9, 936-196-8, 214-277-2 and 203-419-9. ECHA acknowledges your intention. As indicated in your comments, this strategy relies essentially on data, which is yet to be generated, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

5.3. Specification of the study design

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

84 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).

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

6. Long-term toxicity testing on aquatic invertebrates

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

6.1. Information provided

87 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided following information:

(i) Justification: *In accordance with column 2 of REACH Annex IX, long term toxicity testing on aquatic invertebrates (required in section 9.1.5) shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on aquatic organisms. As the substance is not classified as dangerous for the environment, is readily biodegradable and has a low potential for bioaccumulation, no further testing is required.*

6.2. Assessment of the information provided

6.2.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study

88 Under Annex IX, Section 9.1., Column 2 is not a basis for omitting information on long-term toxicity to aquatic invertebrates referred to under Column 1, Section 9.1.5.

89 Your adaptation is therefore rejected.

6.3. Comments on the draft decision

90 In your comments to the draft decision you stated that you want to adapt this information requirement by using a grouping and read-across approach under Annex XI, Section 1.5.

91 You provided a new read-across justification document with your comments.

92 You explain that you intend to predict the properties of the Substance from information to be obtained from the following source substance:

- Reaction mass of diisobutyl adipate and diisobutyl glutarate and diisobutyl succinate (EC 907-870-9) COASOL;

93 You provide the following reasoning for the prediction of *aquatic toxicity*: ”The structural similarity between these two substances and the coherence in existing data regarding relevant properties indicates that the read-across possible, and the data on COASOL will provide a conservative value for reading across to dimethyl adipate and filling the data gap.”.

94 ECHA understands that your read-across hypothesis as described in your comments assumes that different compounds have the same type of effects. You predict the properties of your Substance based on a worst-case approach.

95 Based on the new information provided in your comments (read-across justification for long-term aquatic toxicity), the read-across approach might be plausible for this information requirement. However, the study on the source substance has not been performed yet.

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

97 Therefore, the information requirement is not fulfilled.

7. Long-term toxicity testing on fish

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

7.1. Information provided

99 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided following information:

(i) Justification: *In accordance with column 2 of REACH Annex IX, long term toxicity testing on fish (required in section 9.1.6) shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on aquatic organisms. As the substance is not classified as dangerous for the environment, is readily biodegradable and has a low potential for bioaccumulation, no further testing is required.*

7.2. Assessment of the information provided

7.2.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study

100 Under Annex IX, Section 9.1., Column 2 is not a basis for omitting information on long-term toxicity to fish referred to under Column 1, Section 9.1.6.

101 Your adaptation is therefore rejected.

7.3. Comments on the draft decision

102 In your comments to the draft decision you state that you want to adapt this information requirement by using a grouping and read-across approach under Annex XI, Section 1.5.

103 You provided a new read-across justification document in your comments.

104 You explain that you intend to predict the properties of the Substance from information to be obtained from the following source substance:

- Reaction mass of diisobutyl adipate and diisobutyl glutarate and diisobutyl succinate (EC 907-870-9) COASOL;

105 You provide the following reasoning for the prediction of *aquatic toxicity*: ”The structural similarity between these two substances and the coherence in existing data regarding relevant properties indicates that the read-across possible, and the data on COASOL will provide a conservative value for reading across to dimethyl adipate and filling the data gap.”.

106 ECHA understands that your read-across hypothesis as described in your comments assumes that different compounds have the same type of effects. You predict the properties of your Substance based on a worst-case approach.

107 Based on the new information provided in your comments (read-across justification for long-term aquatic toxicity), the read-across approach might be plausible for this information requirement. However, the study on the source substance has not been performed yet.

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

109 Therefore, the information requirement is not fulfilled.

7.4. Study design and test specifications

110 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 25 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 requests.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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

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

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

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

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

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

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

Appendix 4: Conducting and reporting new tests for REACH purposes

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

1.1. Test methods, GLP requirements and reporting

(1) Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

(2) Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[2].

(4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2. Test material

(1) Selection of the Test material(s)

- 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.

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

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