~~Confidential~~

Helsinki, 26 October 2023

Addressee(s)
Registrant(s) of JS_28472971_FEUC as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
19 May 2017

Registered substance subject to this decision ("the Substance")
Substance name: Diisodecyl azelate
EC/List number: 249-044-4

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit information under request 4. below by ***2 February 2026*** and all other information listed below by ***1 February 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. *In vitro* micronucleus study (Annex VIII, Section 8.4.2., test method: OECD TG 487). The aneugenic potential of the Substance must be assessed with an additional control group for aneugenicity on top of the control group for clastogenicity, if the Substance induces an increase in the frequency of micronuclei.

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

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

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).

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

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

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

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

Information required depends on your tonnage band

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

In the requests above, the same study has been requested under different Annexes. This is because some information requirements may be triggered at lower tonnage band(s). In such cases, only the reasons why the information requirement is triggered are provided for the lower tonnage band(s). For the highest tonnage band, the reasons why the standard information requirement is not met and the specification of the study design are provided. Only one study is to be conducted; all registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the others under Article 53 of REACH.

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report, where** relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the request(s)
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons for the request(s)

Contents

Reasons common to several requests

0.1. Read-across adaptation rejected

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

- *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- *In vitro* micronucleus study (Annex VIII, Section 8.4.2.)
- Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study, one species (Annex IX, Section 8.7.2.)

2 In addition, you have provided a weight of evidence adaptation under Annex XI, Section 1.2 for the following standard information requirement for which you have included a study on analogue whose reliability must be assessed under Annex XI, Section 1.5:

- Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)

3 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.

4 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.

5 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. Predictions for toxicological properties

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

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

- bis(8-methylnonyl) adipate, EC 248-299-9 (source substance 1);
- bis(2-ethylhexyl) adipate, EC 203-090-1 (source substance 2);
- bis(2-ethylhexyl) azelate, EC 203-091-7 (source substance 3);
- dibutyl adipate, EC 203-350-4 (source substance 4).

8 You provide the following reasoning for the prediction of toxicological properties: "the similarity of all analogue/source substances as listed in Table 1 is justified on the basis of the physico-chemical properties, toxicological profiles and supported by various QSAR methods. There is convincing evidence that these chemicals possess an overall common profile, respectively and therefore are suitable for a read across approach".

9 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.

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

10 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.).

11 Supporting information must include supporting information (bridging studies) to compare properties of the category members.

12 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).

13 For the source substances, you provide the studies used in the prediction in the registration dossier. Apart from those studies, your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data for the Substance that would confirm that both substances cause the same type of effects. In particular, you provided no study on the target substance relevant to the adapted information requirements with e.g. lower shorter exposure duration (bridging study).

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

0.1.2. Conclusion on the read-across approach

15 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

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

1.1. Information provided

17 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 (2004) with the source substance Bis(2-ethylhexyl) azelate, EC 203-091-7;

(ii) an *in vitro* gene mutation study in bacteria (2010) with the source substance dibutyl adipate, EC 203-350-4;

1.2. Assessment of the information provided

1.2.1. Read-across adaptation rejected

18 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.

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

19 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 471. Therefore, the following specifications must be met:

a) the test is performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101);

20 In study(ii):

a) the tests were performed with the strains S. typhimurium TA 1535, TA 1537, TA 1538, TA 98 and TA 100 (i.e., the *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) is missing);

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

22 Therefore, the information requirement is not fulfilled.

1.3. Study design

23 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* micronucleus study

24 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.

2.1. Information provided

25 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 (2004) with the source substance Bis(2-ethylhexyl) azelate, EC 203-091-7;

2.2. Assessment of the information provided

2.2.1. Read-across adaptation rejected

26 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.

27 Therefore, the information requirement is not fulfilled.

2.3. Study design

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

2.3.1. Assessment of aneugenicity potential

29 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.

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

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

3. Long-term toxicity testing on fish

31 Short-term toxicity testing on fish is an information requirement under Annex VIII, Column 1, Section 9.1.3. However, long-term toxicity testing on fish may be required by the Agency

(Section 9.1.3., Column 2) if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

3.1. Triggering of the information requirement

32 In the provided study according to EU Method A.6 (2010), the saturation concentration of the Substance in water was determined to be < 0.05 mg/L.

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

3.2. Information requirement not fulfilled

34 The information provided, its assessment and the specifications of the study design are addressed under request 7 (Long-term toxicity testing on fish).

Reasons related to the information under Annex IX of REACH

4. Sub-chronic toxicity study (90 days)

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

4.1. Information provided

36 You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.2. of REACH (weight of evidence), based on the following study records:

(i) Short-term (28-day) toxicity study, 1970, OECD TG 407, with the source substance bis(8-methylnonyl) adipate, EC 248-299-9;

(ii) Short-term (28-day) toxicity study, ,OECD TG 407, with the source substance bis(2-ethylhexyl) adipate, EC 203-090-1;

(iii) Screening study, 2003, OECD TG 422, with the source substance bis(2-ethylhexyl) adipate, EC 203-090-1;

(iv) One-generation study, 1988, OECD TG 415, with the source substance bis(2-ethylhexyl) adipate, EC 203-090-1.

37 You have also 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:

(v) a sub-acute toxicity study (1982) in rats with the source substance bis(2-ethylhexyl) adipate, EC 203-090-1;
(vi) a sub-acute toxicity study (1982) in mice with the source substance bis(2-ethylhexyl) adipate, EC 203-090-1.

38 Finally, you have adapted this information requirement by using Annex IX, Section 8.6.2., Column 2. To support the adaptation, you have provided the following information claiming low toxicological activity:

(i) Substance is unreactive, insoluble, not inhalable and there is no evidence of absorption and no evidence of toxicity based on an oral subacute repeated dose study on the structural analogue diisodecyl adipate (Cas No. 27178-16-1);

(ii) Systemic absorption and human exposure of the substance can not generally be excluded;

(iii) Animal welfare consideration.

4.2. Assessment of the information provided

4.2.1. Rejection of weight of evidence adaptation

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

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

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

4.2.1.1. Lack of documentation justifying the weight of evidence adaptation

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

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

44 Beside this critical deficiency, ECHA has also assessed the other aspects of your adaptation.

4.2.1.2. Issues related to the information provided

45 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.6.2 at Annex IX includes, at general level, information on systemic toxicity in intact, non-pregnant and young adult males and females from: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity. Information should address effects on the following physiological systems: circulatory system, digestive/excretory system, endocrine system, immune system, integumentary system, musculoskeletal system, nervous system, renal/urinary system, reproductive system, and respiratory system.

1) in-life observations and 2) blood chemistry

46 Sources of information (i-ii) provide information on in-life observations and blood chemistry, sources of information (iii-iv) do not because sources of information (iii-iv) are designed for reproductive toxicity assessment, focussing on reproductive organs and fertility issues, and they do not provide relevant information on aspects of in life observations and blood chemistry to address the relevant physiological systems (circulatory, digestive/excretory, integumentary, musculoskeletal, nervous, renal/urinary, and respiratory). Sources of information (i-ii) have the following deficiencies affecting their contribution to the derivation of reliable conclusions:

47 First, 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.

48 Second, you have provided two 28-day toxicity studies conducted with the source substances bis(8-methylnonyl) adipate, EC 248-299-9, and bis(2-ethylhexyl) adipate, EC 203-090-1. These studies do not have the exposure duration of 90 days as required in OECD TG 408.

49 The conditions of exposure in accordance with the OECD TG 408 specifies that dosing of the Substance is performed daily for a period of 90 days until the scheduled termination of the study. This condition of exposure is essential, as the effects observed in a sub-chronic study might be considerably more pronounced compared to a shorter study duration such as a 28-day study. You have not demonstrated that the effects of the Substance generated

over the exposure of 90 days will not be different to that over the exposure of 28 days. Therefore, these studies (i) and (ii) do not inform on the properties of the Substance after a longer exposure than 28 days.

3) organ and tissue toxicity

50 Sources of information (i-ii) provide information on organ and tissue toxicity, sources of information (iii-iv) only very limited information because, as reproductive toxicity studies, they do not cover, for example, relevant histopathological examinations of non sexual organs, including e.g. brain, thyroid, liver, kidney.

51 In addition, the reliability of the sources of information (i-iv) is also affected by the following issue:

52 First, sources of information (i-ii) have the reliability issues identified above under points 1) and 2).

53 Second, in relation to sources of information (iii-iv), 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.

54 In summary, sources of information (i-ii) do not cover all key information of OECD TG 408, while sources of information (iii-iv) cover only very limited organ and tissue toxicity and not other key information, and even for the elements covered they have significant reliability issues and cannot be considered a reliable source of information that could contribute to the conclusion investigated by the required study.

55 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for sub-chronic toxicity study (90 days).

56 Based on the above, your adaptation is rejected.

4.2.2. Rejection of read-across adaptation

57 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. Based on the above, your adaptations is rejected.

4.2.3. Rejection of Column 2 adaptation

58 Under Annex X, Section 8.7., Column 2, the study does not need to be conducted if the following criteria are met:

- the substance is of low toxicological activity, demonstrated by a comprehensive and informative dataset showing no toxicity in any of the tests available; and
- that it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure; and
- that there is no or no significant human exposure.

59 In relation to the first bullet point: you provide no study on repeated dose toxicity with the substance. Therefore, it is not possible for ECHA to conclude on systemic toxicity.

60 In relation to the second point, you state that "There are no studies available in which the toxicokinetic behaviour of diisodecyl azelate (CAS 28472-97-1) has been investigated". Thus, no toxicokinetic data was provided to show that there is no systemic absorption.

61 The uses of the Substance include PROC 4- 9, PROC 13-15, at dedicated and non-dedicated facilities, where "opportunity for exposure arises" and no exposure scenarios are provided in the dossier.

62 You have not provided toxicokinetic data showing that no systemic absorption occurs via relevant routes of exposure.

63 You have not demonstrated no or no significant human exposure, in particular considering the PROCs identified above.

64 On this basis, you have not demonstrated that the criteria for this adaptation are fulfilled.

65 Based on the above, your adaptation is rejected.

66 Therefore, the information requirement is not fulfilled.

4.3. Specification of the study design

67 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.

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

68 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

69 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

70 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 rats (1988) with the source substance bis(2-ethylhexyl) adipate, EC 203-090-1.

5.2. Assessment of the information provided

5.2.1. Read-across adaptation rejected

71 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.

72 Therefore, the information requirement is not fulfilled.

5.3. Study design

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

74 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).

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

6. Long-term toxicity testing on fish

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

6.1. Information provided

77 You have adapted this information requirement and in support of your adaptation, you provide the following justification:

(i) No potential for aquatic toxicity based on the results of short term studies;

(ii) Ready biodegradability expected to result in unlikelihood of chronic exposure;

(iii) P and B criteria not fulfilled, excluding the need for chronic testing based on ECHA guidance;

(iv) Animal welfare.

6.2. Assessment of information provided

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

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

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

80 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 (Decision of the Board of Appeal in case A-011-2018).

81 Your justification to omit this information provided under (i) – (iv) 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.

82 In addition, with regard to the argument under (i) about lack of potential for aquatic toxicity, we note that at present no compliant information on short-term toxicity to fish is provided in your dossier, as the Substance is poorly water soluble.

83 Finally, 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.

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

6.3. Study design

85 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.).

86 The Substance is difficult to test due to the low water solubility (0.05 mg/L) and adsorptive properties (log K_{ow} > 10 and log Koc in a range 6.3 - 7.11 – values estimated with provided QSAR calculations). OECD TG 210 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not

within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 210. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

87 For multi-constituents/UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key constituents or groups of constituents).

88 If you decide to use the Water Accommodated Fraction (WAF) approach, in addition to the above, you must:

- use loading rates that are sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (Guidance on IRs and CSA, Appendix R.7.8.1-1, Table R.7.8-3);
- provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any remaining non-dissolved test material including a justification for the separation technique);
- prepare WAFs separately for each dose level (i.e. loading rate) and in a consistent manner.

Reasons related to the information under Annex X of REACH

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

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

7.1. Information provided

90 You have adapted this information requirement by using Annex X, Section 8.7., Column 2. To support the adaptation, you have provided the following information:

(i) Low toxicological activity based on an oral subacute repeated dose study with the structural analoguous diisodecyl adipate (CAS No. 27178-16-1)

(ii) Systemic absorption and human exposure of the Substance can not generally be excluded but the expected metabolism of the Substance, based on theoretical considerations, is not expected to cause toxicity.

(iii) Animal welfare consideration.

7.2. Assessment of the information provided

7.2.1. Criteria for the application of the adaptation for Annex X, Section 8.7., Column 2 not met

91 Under Annex X, Section 8.7., Column 2, the study does not need to be conducted if the following criteria are met:

- that it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure; and
- that there is no or no significant human exposure.

92 In IUCLID section 7.8.2 you state that "Systemic absorption and human exposure of the substance can not generally be excluded." You mention theoretical metabolism considerations to dismiss the above considerations, but they are not relevant under Column 2.

93 On this basis, you have not demonstrated that the criteria for this adaptation are fulfilled.

94 Based on the above, your adaptation is rejected.

95 Therefore, the information requirement is not fulfilled.

7.3. Study design

96 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species. The study in the first species was carried out by using a rodent species (rat).

97 Therefore, a PNDT study in a second species must be performed in the rabbit as preferred non-rodent species.

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

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

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).
Guidance for monomers and polymers; ECHA (2012).
Guidance on intermediates; ECHA (2010).
All guidance documents are available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF); ECHA (2017).
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs; ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: Procedure

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

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 11 August 2022.

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

ECHA did not receive any comments within the commenting period.

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]

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

Appendix 4: Conducting and reporting new tests for REACH purposes

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

1.1 Test methods, GLP requirements and reporting

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

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

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries (https://echa.europa.eu/practical-guides).

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

1.2 Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

(1) Selection of the Test material(s)

The Test Material used to generate the new data must be selected taking into account the following:

- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/group of constituents on the test results for the endpoint to be assessed. For example, if a constituent/group of constituents of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/group of constituents.

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

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

- The reported composition must also include other parameters relevant for the property to be tested.

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).