~~Confidential~~

Helsinki, 03 May 2023

Addressees
Registrants of JS_33619-92-0 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
22/03/2018

Registered substance subject to this decision ("the Substance")
Substance name: Sodium O,O-di-sec-butyl dithiophosphate
EC number: 251-598-7

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 ***10 August 2026.***

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

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

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

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

3. 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

4. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487);

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

6. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days) requested below (Annex VIII, Section 8.6.1.);

7. 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;
8. 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

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

10. 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);

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

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

The reasons for the decision(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.

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

0. Reasons common to several requests

0.1. Assessment of the read-across approach

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 cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.);
- 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.);
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1);
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.);
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.).

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

4 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.

5 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.

6 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

7 You have provided a justification document for the read-across under section 13 of IUCLID.

8 You predict the properties of the Substance from information obtained with the following source substance: Sodium O,O-diisobutyl dithiophosphate (EC: 258-508-5), hereafter, referred as source substance 1 (IBP1-Na).

9 In addition, under section 7.5.1. (repeated dose toxicity) of IUCLID you have reported studies (28-day) with following analogue substances:

- source substance 2 (NPP1-Na): Phosphorodithioic acid, O,O-dipropyl ester, sodium salt (1:1) (CAS 42401-77-4)
- source substance 3 (NBP1-Na): Phosphorodithioic acid, O,O-dibutyl ester, sodium salt (1:1) (CAS 36245-44-0)

10 You provide the following reasoning for the prediction of toxicological properties from source substance 1 (IBP1-Na): you claim that *"Source and target substances are very similar in*

chemical structure" and the similarity "*reflects the almost identical physico-chemical properties significant for environmental and toxicochemical assessment*". In addition, in order to support your hypothesis, you state that "*based on the data obtained with similar dialkyl-dithiophosphate insecticides both substances are expected to result in identical and or very similar metabolites".* You conclude that "*besides the marginal structural differences in the alkyl chain of the ester (isopropyl versus isobutyl) indicating already a very similar toxicity profile also the mode of action determined by local tissue damage at high test concentration (compromising the tissue buffer capacity) and a comparable metabolism supports the read across and a reliable prediction of the toxicity from the source substance to the target substance".*

11 In your comments to the draft decision you have provided an updated read-across justification document and added an extra source substance: Sodium O,O-diethyl dithiophosphate (EC: 222-079-2) (EP1-Na), hereafter referred as *source substance 5.* You provide the following reasoning for the prediction of toxicological properties, covering both source substance 1 and source substance 5: you claim that the substances "*share the same core structure: the dithiophosphate ester",* they "*distinguish only in the nature of the alkyl groups attached to the dithiophosphate core structure"*. You conclude that as this is the only difference "*the structural similarity, which is a prerequisite for any read across is clearly given".*

12 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.

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

0.1.1.1. Absence of read-across documentation regarding source substance 2 (NPP1-Na) and source substance 3 (NBP1-Na).

14 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must include an explanation why the properties of the Substance may be predicted from information on the source substance(s).

15 You have provided robust study summaries for repeated dose (short-term) toxicity conducted with other substances than the Substance in order to comply with the REACH information requirements.

16 However, you have not provided documentation as to why this information is relevant for the Substance and thus why the properties of the Substance may be predicted from information on the source substances 2 (NPP1-Na) and 3 (NBP1-Na).

17 In the absence of such documentation, the properties of the Substance cannot be reliably predicted from the data on the source substance(s).

18 In the comments to the draft decision you have not provided any new information to address this deficiency.

0.1.1.2. Missing supporting information to compare the toxicological properties of the Substances with source substance 1 (IBP1-Na) and source substance 5 (EP1-Na)

19 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided.

20 Such documentation must provide supporting information to scientifically justify the read-across explanation for prediction of properties.

21 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.).

22 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).

23 In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance with those of the source substance is necessary to confirm that the substances cause the same type of effects.

24 Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substances).

25 In addition, for supporting arguments involving biotransformation, supporting information should allow establishing the rate and extent of biotransformation to confirm the formation of common metabolites.

26 You have provided the following toxicity studies, all performed with the source substance 1 (IBP1-Na):

(i) *In vitro* gene mutation in bacteria study (2012);

(ii) *In vitro* cytogenicity study in mammalian cells (2012);

(iii) *In vitro* gene mutation in mammalian cells study (2013);

(iv) Screening for reproductive/developmental toxicity study (2013);

(v) Sub-chronic (90-day) toxicity study (2017);

(vi) Prenatal developmental toxicity study (2017).

27 In your updated justification document, attached to your comments to the draft decision, you have provided a new study, performed with source substance 5 (EP1-Na):

(vii) Screening for reproductive/developmental toxicity study (2019).

28 In addition you have compared the toxicological properties using QSAR Toolbox (v.4.2.) profilers and concluded that none of the substances "*possess any functional group considered inherently mutagenic*" as well as they do not contain structural features which indicate any mode of action related to reproductive toxicity.

29 Firstly, ECHA notes that neither in the dossier nor in your comments you have provided any experimental data, in particular bridging studies of comparable design and duration for the Substance. In the absence of such information it is not possible to compare the properties of the Substance and of the source substances 1 and 5 to confirm your hypothesis.

30 Secondly, as you have not provided any experimental data to compare the relevant properties of the Substance and source substance 1 (IBP1-Na) and source substance 5 (EP1-Na), the information from QSAR Toolbox profilers does not constitute, on its own, a reliable basis for establishing similarities in toxicological properties, in particular for systemic and reproductive properties.

31 The complexity of the systemic interactions and the reproductive process and the large number of targets/mechanisms associated with those broad areas of toxicity cannot currently be covered only by computational tools.

32 Finally, you have not provided any experimental data establishing the rate and extent of biotransformation of the Substance and of the source substance 1 (IBP1-Na).

33 Therefore, your supporting argument expressed in your original justification document that the Substance and the source substance 1 (IBP1-Na) are expected to metabolise to "*identical and/or very similar metabolites*" is not substantiated.

34 Based on the above, you have not established that the Substance and the source substances 1 (IBP1-Na) and 5 (EP1-Na) are likely to have similar properties. Therefore you have not provided sufficient supporting information to scientifically justify the read-across.

0.1.2. Predictions for ecotoxicological properties

35 You have provided a justification document for the read-across under section 13 of IUCLID.

36 You predict the properties of the Substance from information obtained with the following source substances:

- Source substance 1 (IBP1-Na): Sodium O,O-diisobutyl dithiophosphate, EC No 258-508-5;
- Source substance 4 (EP1-K): O,O-diethyl ester, potassium salt, CAS No 3454-66-8).

37 You provide the following reasoning for the prediction of ecotoxicological properties from source substance 1(IBP1-Na) and source substance 4 (EP1-K): *"The hypothesis for reading across from Sodium O,O-diisobutyl dithiophosphate [*source substance 1, (IBP1-Na)] *and Potassium O,O-diethyl dithiophosphate [*source substance 4, (EP1-K] *to Sodium O,O-di-sec-butyl dithiophosphate [the Substance] (target) is that data submitted on [*source substances 1 (IBP1-Na) and 4 (EP1-K)] *are reliable and sufficient to cover endpoint for the target. This hypothesis is supported by the_similarities of the chemical structure of the 3 chemicals. [..]"*

38 Furthermore, in the read-across justification document *you state that "Source [source substance 1] and target substances are very similar in chemical structure"* and the similarity *"reflects the almost identical physico-chemical properties significant for environmental and toxicochemical assessment".*

39 *In your comments to the draft decision you have provided an updated read-across justification document and added an extra source substance:* Sodium O,O-diethyl dithiophosphate (EC: 222-079-2) (EP1-Na), hereafter referred as *source substance 5.*

40 You provide the following reasoning for the prediction of ecotoxicological properties, covering both source substance 1 and source substance 5: you claim that the substances "*share the same core structure: the dithiophosphate ester",* they "*distinguish only in the nature of the alkyl groups attached to the dithiophosphate core structure"*.

41 You conclude that as this is the only difference "*the structural similarity, which is a prerequisite for any read across is clearly given".*

42 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects.

43 You predict the properties of your Substance to be quantitatively equal to those of the source substance.

44 We have identified the following issue(s) with the prediction(s) of ecotoxicological properties:

0.1.2.1. Missing supporting information to compare the ecotoxicological properties of the Substances

45 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided.

46 Such documentation must provide supporting information to scientifically justify the read-across explanation for prediction of properties.

47 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.).

48 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).

49 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.

50 Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

51 In order to support your hypothesis, you have provided the following experimental aquatic toxicity data:

52 For short term toxicity to aquatic invertebrates, you have provided the following studies:

(i) Daphnia sp. Acute Immobilisation Test (2013) with the source substance 1;

(ii) Arcartia tonsa acute toxicity test (2003) with source substance 4.

53 For toxicity to algae, you have provided the following study:

(iii) Algal inhibition test (1997) with the source substance 1;

(iv) Marine Algal Growth Inhibition Test (2003) with the source substance 4.

54 For short term toxicity to fish, you have provide the following studies:

(v) Fish acute toxicity test (2004) with the source substance 1.

55 In your comments to the draft decision, you have provided a new study performed with source substance 5 (EP1-Na):

(vi) Fish acute toxicity test (1974) with the source substance 5.

56 In addition you have compared the ecotoxicological properties of the Substance with source substance 1 (IBP1-Na) and source substance 5 (EP1-Na)using QSAR Toolbox (v.4.2.) profilers and concluded the "Aquatic toxicity classification by ECOSAR" profiler, which is coupled with the QSAR programme ECOSAR by EPIWIN (US EPA 2012) identified the structural alert "Esters, Dithiophosphates" in the two query substances.

57 Neither the data set in your dossier nor your comments to the draft decision include any experimental data, in particular bridging studies of comparable design and duration for the Substance, to compare the properties of the Substance and of the source substance 1 (IBP1-Na), source substance 4 (EP1-K) and source 5 (EP1-Na) to support your read-across hypothesis.

58 In addition, as you have not provided any experimental data to compare the relevant properties of the Substance and source substance 1 (IBP1-Na) and souce substance 5 (EPI-Na), information from QSAR Toolbox profilers may provide qualitative information on structural similarities but does not constitute, on its own, a reliable basis for establishing similarities in ecotoxicological properties.

59 In the absence of reliable supporting information relevant for the predicted properties, you have not demonstrated that the structural variation does not affect the predicted ecotoxicological properties.

60 Based on the above, you have not established that the Substance and the source substances are likely to have similar properties.

61 Therefore you have not provided sufficient supporting information to scientifically justify the read-across.

0.2. Conclusions on the read-across approach

62 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substances. Therefore, the read-across approaches do not comply with the general rules as set out in Annex XI, Section 1.5.

Reasons related to the information under Annex VII of REACH

1. In vitro gene mutation study in bacteria

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

1.1. Information provided

64 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:

(i) *In vitro* gene mutation in bacteria study (2012) with the source substance 1 (IBP1-Na).

1.2. Assessment of the information provided

65 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 and the information requirement is not fulfilled.

1.3. Specification of the study design

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

2. Short-term toxicity testing on aquatic invertebrates

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

2.1. Information provided

68 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:

(i) Daphnia sp. Acute Immobilisation Test (2013) with the source substance 1 (IBP1-Na);

(ii) Arcartia tonsa acute toxicity test (2003) with the source substance 4 (EP1-K).

2.2. Assessment of the information provided

69 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 and the information requirement is not fulfilled.

2.3. Study design and test specifications

70 The Substance is difficult to test due to the high adsorption potential (ionisable, pKa 7.63). OECD TG 202 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.

71 Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations.

72 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 202.

73 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.

3. Growth inhibition study aquatic plants

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

3.1. 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 the following experimental data:

(i) Algal inhibition test (1997) with the with the the source substance 1 (IBP1-Na);

(ii) Marine Algal Growth Inhibition Test (2003) with the source substance 4 (EP1-K).

3.2. Assessment of the information provided

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 and the information requirement is not fulfilled.

3.3. Study design and test specifications

77 OECD TG 201 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test.

78 Therefore, you must fulfil the requirements described in 'Study design and test specifications' under Request 2.

Reasons related to the information under Annex VIII of REACH

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

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

4.1. 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:

(i) An *in vitro* cytogenicity study in mammalian cells (2013) with the source substance 1 (IBP1-Na)

4.2. Assessment of the information provided

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 and the information requirement is not fulfilled.

4.3. Specification of the study design

82 To fulfil the information requirement for the Substance, either in vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

5. In vitro gene mutation study in mammalian cells

83 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.

5.1. Triggering of the information requirement

84 Your dossier contains (I) a negative result for *in vitro* gene mutation study in bacteria and (II) *in vitro* cytogenicity study in mammalian cells.

85 The *in vitro* gene mutation study in bacteria and the *in vitro* cytogenicity study in mammalian cells provided in the dossier is rejected for the reasons provided in requests 1 and 4.

86 The result of the requests 1 and 4 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.

~~87~~ Consequently, you are required to provide information for this information requirement, if the *in vitro* gene mutation study in bacteria and the *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study provides a negative result.

5.2. Information provided

88 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:

(i) In vitro gene mutation in mammalian cells study (2013) with the source substance 1 (IBP1-Na).

5.2. Assessment of the information provided

89 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 and the information requirement is not fulfilled.

5.3. Specification of the study design

90 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.

6. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days)

91 Annex VIII, Section 8.6.1., Column 2 provides that an experimental study for this information requirement is not needed if a reliable sub-chronic (90 days) or chronic toxicity study is available.

6.1. Information provided

92 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:

(i) Sub-chronic (90-day) repeated dose toxicity study in rats (key study, 2017), performed with source substance 1 (IBP1-Na);

(ii) Screening for reproductive/developmental toxicity study (key stidy, 2013), performed with source substance 1 (IBP1-Na);

(iii) Short-term toxicity (28-day) (supporting, 1989) performed with source substance 2 (NPP1-Na);

(iv) Short-term toxicity (28-day) (supporting, 1989) performed with source substance 3 (NBP1-Na).

6.2. Assessment of the information provided

6.2.1. Grouping and read across approach

93 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.

94 In addition, the source studies (ii) to (iv) have the following issue:

6.2.2. Source study not adequate for the information requirement

95 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 study that shall normally be performed for a particular information requirement, in this case OECD TG 408.

96 Therefore, the following specifications must be met: dosing of the Substance is performed daily for a minimum of 90 days.

97 Study (ii) is described as a screening for reproductive/developmental toxicity study and has been conducted using the OECD TG 422. Studies (iii) and (iv) are described as short-term toxicity studies, conducted using the OECD TG 407.

98 The exposure duration was limited to 44 days for males and to 51 or 56 days.for females under the conditions of study (ii), and to 28 days under the conditions of studies (iii) and (iv).

99 Therefore, the information provided from these studies does not cover the specifications required by the OECD TG 408.

100 Based on the above, the studies (ii) – (iv) do not provide an adequate and reliable coverage of the key parameter(s) addressed by the OECD TG 408.

6.2.3. Column 2 criterion to omit the study is not met

101 Based on the reasons explained in section 6.2.1. and 6.2.2 above, the studies i.-iv. which you may have submitted with a view to omit this information requirement based on Section 8.6.1., Column 2 of Annex VIII to REACH are not considered as reliable sub-chronic studies.

102 Therefore, your adaptation according to Section 8.6.1., Column 2 is rejected and the information requirement is not fulfilled.

6.3. Specification of the study design

103 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see information requirement section 6). 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 therefore need to be conducted.

104 Because you still must comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to submit a justification for the adaptation provided in Column 2 of that provision.

105 In your comments to the draft decision you asked for further guidance relating to the data sharing aspects.

106 Determination of data sharing conditions is subject to freedom to contract. ECHA, as regulatory agency, is not in a position to interfere into registrants' freedom to contract. However, a guidance has been developed on data sharing principles under REACH based on experience of Industry and/or authorities. We encourage you to consult ECHA Guidance on data sharing.

7. Screening for reproductive/developmental toxicity

107 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.

7.1. Information provided

108 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:

(i) Screening for reproductive/developmental toxicity study (2013), performed with the source substance 1 (IBP1-Na).

109 In the comments to the draft decision you have provided a new study, performed with source substance 5 (EP1-Na):

(ii) Screening for reproductive/developmental toxicity study (2019)

7.2. Assessment of the information provided

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

7.3. Specification of the study design

111 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.

112 The study must be conducted with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

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

114 Note that in your comments to the drfat decision you seem to have confused request 6 (Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90)) with the current request, where screening for reproductive/developmental toxicity study is required.

8. Short-term toxicity testing on fish

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

8.1. Information provided

116 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:

(i) Fish acute toxicity test (2004) with the the source substance 1 (IBP1-Na).

117 In your comments to the draft decision, you have provided a new study performed with source substance 5 (EP1-Na):

(ii) Fish acute toxicity test (1974).

8.2. Assessment of the information provided

118 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 and the information requirement is not fulfilled.

8.3. Study design and test specifications

119 OECD TG 203 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design and test specifications' under Request 2.

120 In the comments to the draft decision, you note that the draft decision is requesting both the short and long term study on fish and 'is neither addressing the option to replace the acute by a chronic fish study, nor the related cost sharing aspects'.

121 You propose that the request for short term study is deleted and all registrants in the volume band greater than 10t/y should share the cost of the chronic study, as you consider that Annex VIII dossier would be incomplete without the long-term study.

122 ECHA highlights that short-term study on fish is a standard information requirement at Annex VIII level while long-term study on fish is a standard information requirement at Annex IX level, and as there are data gaps the studies are requested at the respective tonnage levels.

123 The short-term study on fish has its importance for the purpose of acute classification under the CLP Regulation and will fulfil relevant REACH requirements at Annex VIII level.

124 Nevertheless, Annex VIII, section 9.1.3. column 2 provides an adaptation option to the standard information requirement, if a long-term aquatic toxicity study on invertebrates is available.

125 As already noted above under request 6, ECHA, as regulatory agency, is not in a position to interfere into registrants' freedom to contract regarding potential data sharing arrangements.

Reasons related to the information under Annex IX of REACH

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

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

9.1. Information provided

127 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:

(i) Sub-chronic (90-day) repeated dose toxicity study in rats (key study, 2017), performed with the source substance 1 (IBP1-Na).

9.2. Assessment of the information provided

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 and the information requirement is not fulfilled.

9.3. Specification of the study design

129 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.

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

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

10. Pre-natal developmental toxicity study in one species

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

10.1. Information provided

133 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:

(i) Prenatal developmental toxicity study (2017), performed with the source substance 1 (IBP1-Na).

10.2. Assessment of the information provided

134 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 and the information requirement is not fulfilled.

10.3. Specification of the study design

135 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species.

11. Long-term toxicity testing on aquatic invertebrates

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

11.1. Information provided

137 You have provided the following justification to omit the study: "*No further investigation on effects on aquatic organisms is considered necessary because the chemical safety assessment has shown that there is no exposure*."

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

138 A registrant may only adapt this information requirement based on the general rules set out in Annex XI. 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 on aquatic invertebrates under Column 1 (Decision of the Board of Appeal in case A-011-2018).

139 In your justification you do not refer to any of the general adaptation rules. You mention "*no exposure*", but you do not provide any adequate justification and documentation for exposure driven testing in the meaning of Annex XI, Section 3[2].

140 Therefore, you have not demonstrated that the required standard information can be omitted and the information requirement is not fulfilled.

11.2. Study design and test specifications

141 OECD TG 211 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test.

142 Therefore, you must fulfil the requirements described in 'Study design and test specifications' under Request 2.

12. Long-term toxicity testing on fish

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

12.1. Information provided

144 You have provided the following justification to omit the study: *"No further investigation on effects on aquatic organisms is considered necessary because the chemical safety assessment has shown that there is no exposure."*

[2] Guidance on information requirements and chemical safety assessment Chapter R.5: Adaptation of information requirements.

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

145 A registrant may only adapt this information requirement based on the general rules set out in Annex XI. 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 on long-term toxicity to fish under Column 1 (Decision of the Board of Appeal in case A-011-2018).

146 In your justification you do not refer to any of the general adaptation rules. You mention "*no exposure*", but you do not provide any adequate justification and documentation for exposure driven testing in the meaning of Annex XI, Section 3[2].

147 Therefore, you have not demonstrated that the required standard information can be omitted and the information requirement is not fulfilled.

12.2. Study design and test specifications

148 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.).

149 OECD TG 210 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test.

150 Therefore, you must fulfil the requirements described in 'Study design and test specifications' under Request 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 01 February 2022.

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

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

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: Addressees 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[3].

(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 and other parameters relevant for the property to be tested.

This information is needed to assess 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[4].

[3] https://echa.europa.eu/practical-guides
[4] https://echa.europa.eu/manuals