~~Confidential~~

Helsinki, 03 May 2023

Addressee
Registrant of JS_27205-99-8 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
04/04/2018

Registered substance subject to this decision ("the Substance")
Substance name: Sodium O,O-diisopropyl dithiophosphate
EC/List number: 248-322-2

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 ***12 May 2025***.

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. Short-term repeated dose toxicity (28 days; Annex VIII, Section 8.6.1.) to be combined with the Screening for reproductive/developmental toxicity below;

7. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: 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).

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.

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

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.);
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.);
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.);
- 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 standard information requirements in the following sections.

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

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

0.1.1. Predictions for toxicological properties

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

6 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).

7 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).

8 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".

9 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.*

10 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".

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

20 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.).

21 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).

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

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

24 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 needs to be provided.

25 You have provided the following toxicity studies, all performed with the source substances:

(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);

26 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).

27 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.

28 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 substance 1 and to confirm your hypothesis.

29 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 do not constitute, on their own, a reliable basis for establishing similarities in toxicological properties, in particular for systemic and reproductive properties. 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.

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

31 Therefore, your 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.

32 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

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

34 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).

35 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-isopropyl 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. [..]"*

36 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".*

37 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.*

38 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".

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

40 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.

41 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

42 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.

43 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.).

44 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).

45 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.

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

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

48 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.

49 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.

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

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

51 In the 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.

52 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.

53 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 substance 5 (EP1-Na) to support your read-across hypothesis.

54 In addition, as you have not provided any experimental data to compare the relevant properties of the Substance and source substance 1 (IBP1-Na), the 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.

55 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.

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

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

0.2. Conclusions on the read-across approach

58 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

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

1.1. Information provided

60 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

61 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

62 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

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

2.1. 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) 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

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.

2.3. Study design and specifications

66 The Substance is difficult to test due to the high adsorption potential (ionisable, pKa 7.69). 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.

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

68 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.

69 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

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

3.1. Information provided

71 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 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

72 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 specifications

73 OECD TG 201 specifies that, for difficult to test substances, OECD GD 23 must be followed.

74 As already explained above, the Substance is difficult to test.

75 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

76 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

77 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* cytogenicity study in mammalian cells (2013) with the source substance 1 (IBP1-Na).

4.2. Assessment of the information provided

78 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

79 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

80 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

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

82 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.

83 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.

~~84~~ 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

85 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).

5.3. Assessment of the information provided

86 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.

5.4. Specification of the study design

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

88 A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII, Section 8.6.1.

6.1. Information provided

89 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 study, 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).

90 ECHA understands that you have provided the study (i) (sub-chronic toxicity study) in order to omit this information requirement in accordance with Column 2 of Section 8.6.1., of Annex VIII to REACH in conjunction with Annex XI, section 1.5.

6.2. Assessment of the information provided

91 As explained in Section 0.1., your adaptations do not meet the conditions for grouping of substances and read-across approaches under Annex XI, Section 1.5. and are therefore rejected.

92 This applies for studies (ii) – (iv) and equally for study (i) 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 (where a reliably sub-chronic toxicity study (OECD TG 408) is already available).

Therefore, the information requirement is not fulfilled.

6.3. Specification of the study design

93 When there is no information available neither for the 28-day repeated dose toxicity (EU B.7, OECD TG 407), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, Section 8.6.1 and that of REACH Annex VIII, Section 8.7.1. (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

94 For information on the study design see request for OECD TG 422 below.

7. Screening for reproductive/developmental toxicity

95 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

96 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).

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

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

97 Under the Developmental toxicity/teratogenicity section of your technical dossier (IUCLID 7.8.2), you have further provided the following experimental data:

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

98 ECHA understands that you have provided this information in order to adapt this information requirement according to Section 8.7., Column 2 of Annex VIII to REACH in conjunction with Annex XI, section 1.5.

7.2. Assessment of the information provided

99 As explained in Section 0.1., your adaptations do not meet the conditions for grouping of substances and read-across approaches under Annex XI, Section 1.5. and are therefore rejected.

100 This applies for the rejection of studies (i) and (ii), and, equally, for study (iii) which you may have submitted with a view to omit this information requirement based on Section 8.7., Column 2 of Annex VIII to REACH (where an adequate pre-natal developmental toxicity study (OECD TG 414) is already available).

101 Therefore, the information requirement is not fulfilled.

7.3. Specification of the study design

102 A study according to the test method EU B.64/OECD TG 422 must be performed in rats.

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

8. Short-term toxicity testing on fish

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

8.1. Information provided

105 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).

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

106 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

107 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.

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]

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

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[3].

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