~~Confidential~~

Helsinki, 12 October 2023

Addressees
Registrant(s) of JS_68413-48-9 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
31/10/2018

Registered substance subject to this decision ("the Substance")
Substance name: Dibutyl [[bis[(2-ethylhexyl)oxy]phosphinothioyl]thio]succinate
EC number: 270-220-1

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 ***18 April 2028***.

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

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

1. Long-term toxicity testing on aquatic invertebrates (triggered by Annex VII, Section 9.1.1., column 2; test method: EU C.20./OECD TG 211);

2. 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

3. Long-term toxicity testing on fish (triggered by Annex VIII, Section 9.1.3., column 2; test method: EU C.47./OECD TG 210);

4. Soil simulation testing (triggered by Annex VIII, Section 9.2.; test method: EU C.23./OECD TG 307) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.;

5. Sediment simulation testing (triggered by Annex VIII, Section 9.2.; test method: EU C.24./OECD TG 308) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.;

6. Identification of degradation products (triggered by Annex VIII, Section 9.2, Column 2; test method: using test method OECD 307 and OECD 308);

7. Bioaccumulation in aquatic species (triggered by Annex VIII, section 9.3, column 2 test method: EU C.13./OECD TG 305, aqueous exposure/dietary exposure).

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. In addition, the studies relating to biodegradation and bioaccumulation are necessary for the PBT assessment. However, to determine the testing needed to reach the conclusion on the persistency and bioaccumulation of the Substance you should consider the sequence in which these tests are performed and other conditions described in this Appendix.

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 related to the information under Annex VII of REACH

1. Long-term toxicity testing on aquatic invertebrates

1 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII, Column 1, Section 9.1.1.. However, long-term toxicity testing on aquatic invertebrates must be considered (Section 9.1.1., Column 2) if the substance is poorly water soluble.

1.1. Triggering of the information requirement

2 Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests do not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (Guidance on IRs and CSA, Section R.7.8.5).

3 In the provided OECD TG 105 study (2018), the saturation concentration of the Substance in water was determined to be 1.2 µg/L.

4 Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates must be provided.

1.2. Information provided

5 You have provided a short-term toxicity study on aquatic invertebrates but no information on long-term toxicity on aquatic invertebrates for the Substance.

6 Therefore, the information requirement is not fulfilled.

1.3. Study design and test specifications

7 The Substance is difficult to test due to the low water solubility (1.2 µg/L) and adsorptive properties (LogKoc = 8.58 in soil and 8.67 in sludge). The OECD TG 211 specifies that, for difficult to test substances, you must consider the approach described in the 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 the OECD TG 211. 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 solutions.

1.4. Assessment of your comments to the draft decision

8 In your comments to the draft decision, you do not agree to perform the requested study. You have provided output data from QSARs (ECOSAR v. 1.11, "Esters", "Esters, Dithiophosphonates" and "Neutral Organics" classes) in order to adapt the information requirement for long-term toxicity on aquatic invertebrates. In addition, you refer to

physicochemical properties of the Substance and a prediction on partitioning of the Substance in soil and sediment to mitigate potential aquatic toxicity concerns.

1.4.1. (Q)SAR adaptation rejected

9 Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

(1) the prediction needs to be derived from a scientifically valid model,
(2) the substance must fall within the applicability domain of the model,
(3) results need to be adequate for the purpose of risk assessment or classification and labelling, and
(4) adequate and reliable documentation of the method must be provided.

1.4.1.1. The substance is outside the applicability domain of the model

10 Under Guidance on IRs and CSA R.6.1.5.3., a prediction is within the applicability domain of the model, when, among others, the substance falls within the descriptor, structural, mechanistic and metabolic domains.

11 In your comments to the draft decision, you use ECOSAR "Esters", "Esters, Dithiophosphonates" and "Neutral Organics" class specific models. You apply a note attached to the predicted values stating that "may not be soluble enough to measure this predicted effect" ("Esters", "Neutral Organics" models) to explain that there will not be any effects below the water solubility limit of the Substance. In addition, you explain that some substances with high logKow are being excluded from the models for no effects at saturation concentrations ("Neutral Organics", "Esters" models), to further support your claim.

12 We have assessed the provided QSARs and conclude that the Substance is outside of the applicability domain of the models. Therefore, your explanation based on the note and the substances excluded from the models is based on a model output that is not applicable to the Substance. More specifically, the Substance used as input for the prediction is outside the structural domain of the "Neutral organics" and "Esters" models. The Substance contains the distihiophosphate fragment, and those models do not cover the dithiophosphate fragment of the substance.

13 Regarding the "Esters, Dithiophosphate" model, the Substance is out of parametric domain of the model. The logKow of the Substance (extrapolated logKow 7.7, estimated logKow >10) is higher than the maximum logKow covered by the training set (logKow 4.5).

14 Consequently, the provided information does not meet the conditions defined under Annex XI, Section 1.3.

15 Based on the above, your adaptation presented in your comments is rejected.

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

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

17 In your comments to the draft decision, you state that based on the physicochemical properties of the Substance and EPA's Level III Fugacity Model, the Substance would partition primarily in soil and sediment mitigating potential aquatic toxicity concerns.

18 However, the arguments you provide in your comments do not refer to any adaptation possibilities under Annex XI.

19 Based on the above, your justification to omit the study has no legal basis and is rejected.

2. Growth inhibition study aquatic plants

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

2.1. Information provided

21 You have provided a growth inhibition study on algae (2006) with the Substance (study i).

2.1.1. Assessment of the information provided

22 To fulfil the information requirement, a study must comply with OECD TG 201 and the requirements of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

23 Characterisation of exposure

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

24 Additional requirements applicable to difficult to test substances

b) a justification for, or validation of, the separation technique is provided.

25 In study (i) described as growth inhibition study on algae:

26 Characterisation of exposure

a) no analytical monitoring of exposure was conducted and you have not provided a justification whether analytical monitoring is not feasible;

27 Additional requirements applicable to difficult to test substances

b) you have indicated that the test solution was filtered "*through a folded filter which had been previously rinsed with deionized water*" and the "*clear filtrate (eluate) was used directly without further dilution in the algae test*". You have not provided any justification for the separation technique used to prepare the test solution.

In your comments, you provide further information regarding the filtration process (b) and analytical monitoring (a). You state that "*Although the study was conducted without analytical monitoring (quantification) of the substance in the test solution, the registrants maintain that repeating the study solely to obtain a measured concentration would provide no additional information regarding the toxicity of the substance to aquatic plants, as the measured concentration would still represent the maximum water soluble fraction in the test medium, a concentration at which no inhibitory effects on the test organism are observed.*" In addition, you refer to the analytical measurements for the acute toxicity to fish study (OECD 203).

28 Based on the information provided in your dossier and in the comments:

- the Substance is difficult to test since it is poorly water soluble (1.2 µg/L) and there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, you have not provided any justification for the use of filtration as separation method, which can cause losses due to adsorption onto the filter matrix. Regarding analytical measurements from the OECD 203 study to which you refer in your comments, the test media or the technique for preparing the WAFs (siphoning versus filtration) are not comparable to the corresponding

requirements in the OECD TG 201. However, based on the OECD TG 203 study, it is clear that analytical monitoring is feasible, using a liquid chromatography with tandem mass spectrometry detection (LC-MS/MS) method with a limit of quantification (LOQ) of 0.1 µg/L.

- In addition, in the absence of analytical monitoring, it cannot be concluded to what extent the test organisms were exposed to the test substance throughout the exposure. Therefore the effect value based on nominal concentration is not reliable and the hazard can be underestimated.

29 On this basis, the requirements of OECD TG 201 are not met and the information requirement is not fulfilled.

2.2. Study design and test specifications

30 The OECD TG 201 specifies that, for difficult to test substances, the 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 1.

Reasons related to the information under Annex VIII of REACH

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 must be considered (Section 9.1.3., Column 2) if the substance is poorly water soluble.

3.1. Triggering of the information requirement

32 Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests do not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (Guidance on IRs and CSA, Section R.7.8.5).

33 As already explained in Request 1, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

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

3.2. Information provided

35 You have provided a short-term toxicity study on fish but no information on long-term toxicity on fish for the Substance.

3.3. Study design and test specifications

36 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.).

37 The 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. Therefore, you must fulfil the requirements described in 'Study design and test specifications' under Request 1.

3.4. Assessment of your comments to the draft decision

38 In your comments to the draft decision, you do not agree to perform the requested study. Similar to Section 1.2, you have provided output data for QSARs (ECOSAR v. 1.11, "Esters", "Esters, Dithiophosphonates" and "Neutral Organics" classes) in order to adapt the information requirement for long-term toxicity on fish. In addition, you refer to physicochemical properties of the Substance and a prediction on partitioning of the Substance in soil and sediment to mitigate potential aquatic toxicity concerns.

39 For the same reasons as already explained under Section 1.3.1., your adaptation under Annex XI, section 1.3 and your justification with no legal basis are rejected.

40 Therefore, based on the information in the dossier and in your comments, the information requirement is not fulfilled.

4. Soil simulation testing

41 Under Annex VIII, Section 9.2., Column 2, further information on degradation or further testing as described in Annex IX must be generated if the chemical safety assessment (CSA) in accordance with Annex I indicates the need to investigate further the degradation of the substance.

4.1. Triggering of the information requirement

42 Therefore, this information requirement is triggered in case if for example additional information on degradation as set out in Annex XIII, point 3.2.1, is required to assess PBT or vPvB properties of the substance in accordance with subsection 2.1 of that Annex. This is the case if the Substance itself or any of its constituent or impurity present in concentration ≥ 0.1% (w/w) or relevant transformation/degradation product meets the following criteria:

- it is potentially persistent or very persistent (P/vP) as:
  - it is not readily biodegradable (*i.e.* <60% degradation in an OECD 301B);
- it is potentially bioaccumulative or very bioaccumulative (B/vB) as:
  - it has a high potential to partition to lipid storage (*e.g.* log K_{ow} > 4.5).

43 Your registration dossier provides the following PBT/vPvB screening information:

- the Substance is not readily biodegradable (12.1% degradation after 28 days in OECD TG 301B);
- the Substance has a high potential to partition to lipid storage (Log K_{ow} > 6.5 based on OECD TG 117).

44 Furthermore:

- it is not possible to conclude on the bioaccumulation potential of the Substance (see Request 7 of this decision), and
- it is not possible to conclude on the toxicity of the Substance see Requests 1 and 3 of this decision).

45 Under section 2.3 of your IUCLID dossier ('PBT assessment'), you conclude that the Substance is not B/vB because you assume it "*is not expected to be absorbed by fish*".

46 You support this assumption based on the following:

- "*The typical molecular mass of the substance (C28H55O6PS2) is 582.84 Daltons*";
- The Substance is "*highly lipophilic (Log Pow > 5.6)*".

47 You also indicate that the available acute oral toxicity study in rats with the Substance showed LD50 of 11300 mg/kg body weight. In addition, no systemic effects were observed in rats in the available repeated dose oral toxicity study combined with the reproductive/developmental toxicity screening test with the Substance (14-d oral NOEL = 1000 mg/kg/day).

48 Based on the above, ECHA understands that you assume the Substance to be not B/vB based on hindered uptake in fish due to the Substance's properties (large size and lipophilicity).

49 We have assessed the additional information on B/vB in your PBT assessment and identified the following issue.

50 Guidance on IRs and CSA, Section R.7.8.5. explains that there is no scientific basis to define molecular characteristics that would render a substance unlikely to cross biological membranes. In this context, the indicators used for low likelihood of a high bioaccumulation potential (Guidance on IRs and CSA, Section R.11, Figure R.11-4) must be considered, including:

- physico-chemical indicators of hindered uptake due to large molecular size (*e.g.* D_{max} > 17.4 Å and MW > 1100 or MML > 4.3 nm) or high octanol-water partition coefficient (Log K_{ow} > 10) or low potential for mass storage (octanol solubility (mg/L) < 0.002 x MW), and
- supporting experimental evidence of hindered uptake (no chronic toxicity for mammals and birds, no chronic ecotoxicity, no uptake in mammalian toxicokinetic studies, very low uptake after chronic exposure).

51 Your registration dossier provides:

- physico-chemical indicators which you consider supportive of hindered uptake, i.e. MW = 582.84 and LogKow > 6.5 (7.7 based on extrapolation).

52 The available information on the Substance does not support that the Substance is unlikely to cross biological membranes because the physico-chemical indicators for the Substance are below the thresholds listed above and hence they do not indicate low likelihood of B/vB potential.

53 Therefore, the additional information from your PBT assessment is not adequate to conclude that the Substance is not a potential PBT/vPvB substance.

54 Based on the above, the available screening information on the Substance indicates that it is a potential PBT/vPvB substance. Further, the additional information from your PBT assessment is not adequate to conclude on the PBT/vPvB properties of the Substance.

55 Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

56 Further, the Substance has low water solubility (1.2 µg/L) and high adsorption coefficient (log $K_{oc,soil}$ of 8.58), indicating high potential to adsorb to soil.

57 Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation. Based on the adsorptive properties of the Substance, soil represents a relevant environmental compartment.

58 Your registration dossier does not include any information on aerobic and anaerobic biodegradation in soil. Therefore, the information requirement is not fulfilled.

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

4.2. Study design and test specifications

60 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and

2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

61 In accordance with the specifications of OECD TG 307, you must perform the test using at least four soils representing a range of relevant soils (i.e. varying in their organic content, pH, clay content and microbial biomass).

62 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 307.

63 In accordance with the specifications of OECD TG 307, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents (Guidance on IRs and CSA, Section R.7.9.4.1.). By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

64 Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 307; Guidance on IRs and CSA, Section R.11.4.1.).

5. Sediment simulation testing

65 Under Annex VIII, Section 9.2., Column 2, further information on degradation or further testing as described in Annex IX must be generated if the chemical safety assessment (CSA) in accordance with Annex I indicates the need to investigate further the degradation of the substance.

5.1. Triggering of the information requirement

66 Therefore, this information requirement is triggered in case if for example additional information on degradation as set out in Annex XIII, point 3.2.1, is required to assess PBT or vPvB properties of the substance in accordance with subsection 2.1 of that Annex.

67 As already explained in Request 4, the Substance is a potential PBT/vPvB substance.

68 Further, the Substance has low water solubility (1.2 µg/L) and high adsorption coefficient (log $K_{oc,soil}$ of 8.58), indicating high potential to adsorb to sediment.

69 Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation. Based on the adsorptive properties of the Substance, sediment represents a relevant environmental compartment.

70 Your registration dossier does not include any information on aerobic and anaerobic biodegradation in sediment. Therefore, the information requirement is not fulfilled.

71 In your comments to the draft decision, you agree that the study may need to be conducted. You propose a tiered approach where simulation in soil is performed first. ECHA acknowledges your intentions and notes that further guidance is provided below, in Appendix 4, Section 2.1 .

5.2. Study design and test specifications

72 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and

2) a kinetic study where the degradation rate constants (and degradation half-lives)

of the parent substance and of relevant transformation/degradation products are experimentally determined.

73 In accordance with the specifications of OECD TG 308, you must perform the test using two sediments. One sediment should have a high organic carbon content (2.5-7.5%) and a fine texture, the other sediment should have a low organic carbon content (0.5-2.5%) and a coarse texture. If the Substance may also reach marine waters, at least one of the water-sediment systems should be of marine origin.

74 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 308.

75 In accordance with the specifications of OECD TG 308, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents (Guidance on IRs and CSA, Section R.7.9.4.1.). By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

76 Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 308; Guidance on IRs and CSA, Section R.11.4.1.).

6. Identification of degradation products

77 Under Annex VIII, Section 9.2., Column 2, further information on degradation or further testing as described in Annex IX must be generated if the chemical safety assessment (CSA) in accordance with Annex I indicates the need to investigate further the degradation of the substance.

6.1. Triggering of the information requirement

78 Therefore, this information requirement is triggered in case if for example additional information on degradation as set out in Annex XIII, point 3.2.1, is required to assess PBT or vPvB properties of the substance in accordance with subsection 2.1 of that Annex.

79 As already explained in Request 4, the Substance is a potential PBT/vPvB substance.

80 Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

81 Your registration dossier does not include any information on degradation products identity.

6.2. Assessment of your comments to the draft decision

82 In your comments to the draft decision, you do not agree to perform the requested study. You state that in your opinion the trigger according to Annex VIII, column 2 refers to the testing of the substance and therefore the identification of degradation products is not an Annex VIII requirement. However, as stated above, this information requirement as set out

in Annex VIII, Section 9.2., Column 2 refers to the need to investigate further the degradation of the substance. As already confirmed by the Board of Appeal in case A-012-2021, this includes the process of degradation and the identification of the degradation products of the substance. Also, as you have noted yourself in your comments, the requested simulation studies all include identification of degradation products.

83 Therefore, the information requirement is not fulfilled.

6.3. Study design and test specifications

84 To determine the degradation rate of the Substance, the requested studies according to OECD TG 307 and 308 (requests 4 and 5) must be conducted at 12°C and at test material application rates reflecting realistic assumptions. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline) and at higher application rate (*e.g.* 10 times).

7. Bioaccumulation in aquatic species

85 Under Annex VIII, Section 9.3., Column 2, further information on bioaccumulation must be generated if additional information on bioaccumulation as set out in Annex XIII, point 3.2.2, is required to assess PBT or vPvB properties of the substance in accordance with subsection 2.1 of that Annex.

86 As already explained in Request 4, the Substance is a potential PBT/vPvB substance.

87 Your registration dossier does not include any information on bioaccumulation.

7.1. Assessment of your comments to the draft decision

88 In your comments to the draft decision, you do not agree to perform the requested study. You provide output data for a QSAR (BCFBAF v.3.01). Furthermore, you propose to perform an *in vitro* fish metabolism study according to OECD TG 319, and use this information in the Arnot-Gobus model and improve the prediction for determining whether the registered substance is not bioaccumulative or very bioaccumulative without the use of a vertebrate animal species.

7.1.1. (Q)SAR adaptation rejected

89 Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

(5) the prediction needs to be derived from a scientifically valid model,
(6) the substance must fall within the applicability domain of the model,
(7) results need to be adequate for the purpose of risk assessment or classification and labelling, and
(8) adequate and reliable documentation of the method must be provided.

7.1.1.1. The substance is outside the applicability domain of the model

90 Under Guidance on IRs and CSA R.6.1.5.3., a prediction is within the applicability domain of the model, when, among others, the substance falls within the descriptor, structural, mechanistic and metabolic domains.

91 You provide a QSAR, where you apply the BCFBAF model in EPISuite to predict the BCF of the Substance.

92 We have assessed the provided QSARs and the Substance used as input for the prediction is out of descriptor domain. The applied model has a descriptor range of logKow 0.31 – 8.7. You have ran the predictions with the estimated logKow value of 10.98. The predicted LogKow value of 10.98 is out of applicability domain of the model.

7.1.1.2. The prediction is not adequate due to low reliability

93 Under Guidance on IRs and CSA R.6.1.3.4. a prediction is adequate for the purpose of classification and labelling and/or risk assessment when the model is applicable to the chemical of interest with the necessary level of reliability. Guidance on IRs and CSA R.6.1.5.3. specifies that, among others, the following conditions must be met:

- reliable input parameters are used, and
- the model predicts well substances that are similar to the substance of interest,

94 You have also ran the predictions with the extrapolated logKow value of 7.7 from an experimental study. As you state in your comments to the draft decision, there is uncertainty with the extrapolated logKow. You also state that *"an experimental LogKOW value above 10 presents significant technical challenges"* . Therefore, the extrapolated value cannot be considered as a reliable input parameter, making the prediction output unreliable.

95 You have provided predictions that contain analogues (Malathion CAS 121-75-5 and Malaoxon CAS 1634-78-2). However, the analogues have a significantly lower logKow compared (logKow 2.4 for Malathion and logKow 0.5 for Malaoxon) to the Substance (extrapolated log Kow 7.7, predicted logKow 10.98). Furthermore, based on the EPISUITE BCFBAF helpfile (Appendix J. - kM Biotransformation Estimation Method Validation Dataset) the experimental log half-live values for substance Malathion and substance Malaoxon are 0.29 and -1.04 and the half-live values predicted by the model are -2.12 and -3.44, respectively, showing that the values are underestimated by 2 log units. Thus, it is demonstrated that the predicted values for the Substance may not be reliable.

96 In your comments to the draft decision, you acknowledge that the predictions are uncertain and provide the following suggestion to further improve the reliability of the prediction:

97 "*Two important considerations with the above estimates include the uncertainty of the extrapolated LogKOW value of 7.7 and the potential biotransformation rate of the registered substance in fish. EPISuiteTM estimates the LogKOW of the registered substance to be 10.98, which exceeds the LogKOW threshold of > 10 used by ECHA for concluding that a chemical substance has a BCF/BAF "probably lower than 2000 [L/kg wet-wt]". However, obtaining an experimental LogKOW value above 10 presents significant technical challenges. Therefore, the registrants propose to determine the intrinsic clearance in an in vitro rainbow trout liver study, according to OECD TG 319. This information may be used to inform the Arnot-Gobas model and improve the prediction for determining whether the registered substance is not bioaccumulative or very bioaccumulative without the use of a vertebrate animal species.*"

98 ECHA acknowledges your intention to try to further improve the prediction in regards to biotransformation with OECD 319. However, The issues regarding applicability domain described above will not be resolved by the OECD 319.

99 The information in your comments does not change the outcome of this assessment. Therefore, the information requirement is not fulfilled.

7.2. Study design and test specification

100 Bioaccumulation in fish: aqueous and dietary exposure (Method EU C.13 / OECD TG 305) is the preferred test to investigate bioaccumulation (Guidance on IRs and CSA, Section R.7.10.3.1.). Exposure via the aqueous route (OECD TG 305-I) must be conducted unless it can be demonstrated that:

- a stable and fully dissolved concentration of the test material in water cannot be maintained within ± 20% of the mean measured value, and/or
- the highest achievable concentration is less than an order of magnitude above the limit of quantification (LoQ) of a sensitive analytical method.

101 This test set-up is preferred as it allows for a direct comparison with the B and vB criteria of Annex XIII of REACH.

102 You may only conduct the study using the dietary exposure route (OECD 305-III) if you justify and document that testing through aquatic exposure is not technically possible as indicated above. You must then estimate the corresponding BCF value from the dietary test data according to Annex 8 of the OECD 305 TG and OECD Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation (ENV/JM/MONO(2017)16).

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 14 January 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 amended the request(s).

As a result of information provided in your comments considered sufficient and relevant, the request for simulation testing in surface water study was removed from the decision.

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[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.

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

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. General recommendations for conducting and reporting new tests

2.1. Strategy for the PBT/vPvB assessment

Under Annex XIII, the information must be based on data obtained under conditions relevant for the PBT/vPvB assessment. You must assess the PBT properties of each relevant constituent of the Substance present in concentrations at or above 0.1% (w/w) and of all relevant transformation/degradation products. Alternatively, you would have to justify why you consider these not relevant for the PBT/vPvB assessment.

You are advised to consult Guidance on IRs & CSA, Sections R.7.9, R.7.10 and R.11 on PBT assessment to determine the sequence of the tests needed to reach the conclusion on PBT/vPvB. The guidance provides advice on 1) integrated testing strategies (ITS) for the P, B and T assessments and 2) the interpretation of results in concluding whether the Substance fulfils the PBT/vPvB criteria of Annex XIII.

In particular, you are advised to first conclude whether the Substance fulfils the Annex XIII criteria for P and vP, and then continue with the assessment for bioaccumulation. When determining the sequence of simulation degradation testing you are advised to consider the intrinsic properties of the Substance, its identified uses and release patterns as these could significantly influence the environmental fate of the Substance. You must revise your PBT assessment when the new information is available.

[3] https://echa.europa.eu/manuals