~~Confidential~~

Helsinki, 25 August 2021

Addressees
Registrant(s) of JS_ 26741-53-7 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
24/10/2017

Registered substance subject to this decision ("the Substance")
Substance name: 3,9-bis(2,4-di-tert-butylphenoxy)-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5.5]undecane
EC number: 247-952-5
CAS number: 26741-53-7

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 the deadline of ***3 March 2025***.

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

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

1. Water solubility (Annex VII, Section 7.7.; test method: EU A.6./OECD TG 105)

2. Partition coefficient n-octanol/water (Annex VII, Section 7.8.; using an appropriate test method)

3. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. /OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102

4. Long-term toxicity testing on aquatic invertebrates also requested below (triggered by Annex VII, Section 9.1.1., column 2)

5. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201)

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

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

2. Adsorption/ desorption screening (Annex VIII, Section 9.3.1.; test method: EU C.19/OECD 121)

3. Simulation testing on ultimate degradation in surface water also requested below (triggered by Annex VIII, Section 9.2.)

4. Sediment simulation testing also requested below (triggered by Annex VIII, Section 9.2.)

5. Identification of degradation products also requested below (triggered by Annex VIII, Section 9.2.)

6. Bioaccumulation in aquatic species also requested below (triggered by Annex I, Sections 0.6.1. and 4; Annex XIII, Section 2.1.)

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

1. Pre-natal developmental toxicity study in a second species (triggered by Annex IX, Section 8.7.2., column 2; test method: OECD TG 414) by oral route, in a second species (rat)

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

3. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

4. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: EU C.25./OECD TG 309) 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 (Annex IX, Section 9.2.1.4.; 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 (Annex IX, 9.2.3.; test method: OECD TG 308 and 309)

7. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2; test method: OECD TG 305)

Reasons for the request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendix entitled "Reasons to request information required under Annexes VII to X of REACH", respectively.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- 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.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

For certain endpoints, ECHA requests the same study from registrants at different tonnages. In such cases, only the reasoning why the information is required at lower tonnages is provided in the corresponding Appendices. For the tonnage where the study is a standard information requirement, the full reasoning for the request including study design is given. Only one study is to be conducted; the registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the other registrants under Article 53 of REACH.

How to comply with your information requirements

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

You must follow the general testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

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 Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes".

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 Christel Schilliger-Musset, Director of Hazard Assessment

[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 on Reasons common to several requests

1. Assessment of your (Q)SAR adaptation

You seek to adapt the following standard information requirements by applying (a) (Q)SAR approach(es) in accordance with Annex XI, Section 1.3:

i. Water solubility (Annex VII, Section 7.7.)
ii. Partition coefficient n-octanol/water (Annex VII, Section 7.8.)
iii. Adsorption/desorption screeening (Annex VIII, Section 9.3.1.)

You also seek to use QSAR predictions as supporting evidence for your Weight of evidence adaptation under REACH (Annex XI, section 1.2) for the following information requirement:

iv. Bioaccumulation in aquatic species (triggered by Annex I, Sections 0.6.1. and 4; Annex XIII, Section 2.1. and also Annex IX, Section 9.3.2.)

ECHA has considered the scientific and regulatory validity of your (Q)SAR adaptation(s) in general before assessing the specific standard information requirements in the following appendices.

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.

With regard to these conditions, we have identified the following issue:

Lack of or in*adequate documentation of the prediction (QPRF)*

ECHA Guidance R.6.1.6.3 states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:

- the model prediction(s), including the endpoint,
- a precise identification of the substance modelled,
- the relationship between the modelled substance and the defined applicability domain,
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

The documentation provided does not include considerations of the presence and reliability of predictions for close analogues of the Substance in the training set of the different models, including considerations on how predicted and experimental data for analogues support the predictions. Lacking such considerations on close analogues hinders the possibility to assess the reliability of the predictions, especially for models that lack specific correction factors that would account for the presence of the "unusual" eterocyclic P-O fragment at the core of the structure.

In absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.

Additional issues related to (Q)SAR are addressed under the corresponding Appendices.

Appendix A: Reasons to request information required under Annex VII of REACH

1. Water solubility

Water solubility is an information requirement under Annex VII to REACH (Section 7.7.).

You have provided an adaptation under Annex XI, Section 1.3 ('QSAR') with the following supporting information:

i. a water solubility estimate based on the ACD software.

We have assessed this information and, in addition to the deficiency described in the Appendix on reasons common to several requests, we have identified the following additional issue:

Inadequate documentation of the model (QMRF)

Under Appendix C of the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) and ECHA Guidance R.6.1.6.3., adequate and reliable documentation must include a (Q)SAR Model Reporting Format document (QMRF) which reports, among others, the following information:

- the predicted endpoint, including information on experimental protocol and data quality for the data used to develop the model;
- an unambiguous definition of the algorithm, the descriptor(s) of the model and its applicability domain,
- an estimate of the goodness-of-fit and of the predictivity of the model, including information on training set and validation statistics.

You have not provided any of the information listed above.

In absence of such information, ECHA cannot establish that the model can be used to meet this information requirement.

In your comments on the draft decision you provided information (on hydrolysis) to support your justification that the water solubility test could not be conducted. This information addresses the incompliance for a water solubility test. However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

On this basis, the information requirement is not currently fulfilled.

2. Partition coefficient n-octanol/water

Partition coefficient n-octanol/water is an standard information requirement under Annex VII to REACH (Section 7.8.).

You have provided an adaptation under Annex XI, Section 1.3 ('QSAR') with the following supporting information:

i. a Log Kow estimate based on the fragment method from KOWWIN (v1.68).

We have assessed this information and, in addition to the deficiency described in the Appendix on reasons common to several requests, we have identified the following issue:

The substance is outside the applicability domain of the model.

Under ECHA Guidance R.6.1.5.3., a substance must fall within the applicability domain

specified by the model developer.

The applicability domain of the model you used is fragment based. The QPRF you provided correctly lists the correction factors and their occurences in the structure of the Substance. The number of occurrences is then compared to the maximum number of occurrences in the training set of the model to assess whether the structure is within the domain of the model.

Among others, you report the following information for the fragments:
-tert Carbon: max occurences in training set =4; occurences in the substance = 5
>P-: max occurences in training set =1; occurences in the substance = 2
-O-P: max occurences in training set =3; occurences in the substance = 4

The maximum number of occurences for the fragments listed above is exceeded by the predicted structure, which is therefore outside the applicability domain of the model.

Consequently, you have not demonstrated that the Substance falls within the applicability domain of the model.

In your comments on the draft decision you provided information (on hydrolysis) to support your justification that the test could not be conducted. This information addresses the incompliance for a partition coefficient n-octanol/water test. However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

On this basis, the information requirement is not currently fulfilled.

3. In vitro gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

a) Information provided in the dossier

You have provided a key study in your dossier:

i. *In vitro* gene mutation study in bacteria ([redacted] (1977)), reliability 2 with the following strains: TA 98, TA 100, TA 1535, TA 1537, and TA 1538.

We have assessed this information and identified the following issues:

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[2] (1997). One of the key parameters of this test guideline includes:

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

The reported data for the study (i) you have provided did not include:

a) the required fifth strain, S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101).

In your comments on the draft decision you stated that the request for an additional *in vitro* gene mutation study in bacteria is not justified because there are multiple genotoxicity studies available and based on the totality of the evidence, there is no concern for genotoxicity as a

[2] ECHA Guidance R.7a, Table R.7.7–2, p.557

result of exposure to the substance.

We have assessed this information and identified the following issue(s):

1) No legal basis for adaptation

A registrant may only adapt this information requirement based on the specific rules set out under column 2 of Section 8.4.1. or the general rules set out in Annex XI to REACH.

Your justification to omit this information does not explicitly refer to any legal grounds for adaptation under column 2 of Section 8.4.1. or Annex XI to REACH.

This is not a valid adaptation under column 2 of Section 8.4.1. or Annex XI to REACH.

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

In addition, you refer to another *In vitro* gene mutation study in bacteria ([redacted] (1994)) but do not include the details of this study in your comments. Consequently ECHA is not in a position to assess its adequacy to meet the information requirement. You mention that you will provide the information in an updated dossier. ECHA acknowledges that you will update the dossier.

On this basis, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) should be performed using one of the following strains: *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102

4. Long-term toxicity testing on aquatic invertebrates

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

Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests does 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 (ECHA Guidance R.7.8.5).

You have provided the following information which indicates that the Substance is poorly water soluble: all measurements of test media were below the LOQ of 0.02 mg/l in the Daphnia magna reproduction test.

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

In your registration dossier, you have provided a Daphnia magna reproduction test (OECD TG 211), [redacted], 2013.

The examination of this information, as well as the selection of the requested test and the test design are addressed under Appendix C.2.

5. Growth inhibition study aquatic plants

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

You have provided a growth inhibition test on algae (OECD TG 201), [redacted], 2013.

We have assessed this information and identified the following issue:

To fulfil the information requirement, a study must comply with OECD TG 201 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) because the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Characterisation of exposure

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (*i.e.* detection and quantification) and working range must be available. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;

Additional requirements applicable to difficult to test substances

- visual observations is not sufficient to demonstrate that the water solubility limit is reached;
- if the test material is tested at the saturation concentration, evidence must be provided that all reasonable efforts have been taken to achieve a saturation concentration, which include:
  1) an analytical method validation report demonstrating that the analytical method is appropriate, and
  2) information on the saturation concentrations of the test material in water and in the test solution, and
  3) the results of a preliminary experiment demonstrating that the test solution preparation method is adequate to maximize the concentration of the test material in solution;
- the efficacy of the separation method is assessed (*e.g.* by checking for the Tyndall effect or by any other appropriate means);
- a justification for, or validation of, the separation technique is provided;

Your registration dossier provides an OECD TG 201 showing the following:

Characterisation of exposure

- No analytical monitoring of exposure was conducted. You have provided a justification that the concentration of the test chemical in the test solution cannot be analytically measured after the separation of non-dissolved test material because the dissolved concentration is below the limit of detection. You must explain why a lower detection limit could not be achieved.

Additional requirements applicable to difficult to test substances

- The maximum dissolved concentration that can be achieved in the specific test solution under the test conditions was not determined;
- It was not demonstrated that the stock solution preparation method:
  - is of adequate quality (*i.e.* water solubility limit is reached when targeted), and
  - allows to produce reproducible stock solutions (*i.e.* acceptable variation between

preparations);
- Visual observations was used to demonstrate that the water solubility limit is reached;
- You did not provide evidence that all reasonable efforts have been taken to achieve a saturation concentration, which include:
  - an analytical method validation report demonstrating that the analytical method is appropriate, and
  - information on the saturation concentrations of the test material in water and in the test solution, and
  - the results of a preliminary experiment demonstrating that the test solution preparation method is adequate to maximize the concentration of the test material in solution;
- The efficacy of the separation method by filtration has not been assessed;
- A justification for, or validation of, the filtration separation technique has not been provided;

Based on the above,
- there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically the exposure was not characterised;
- the Substance is difficult to test due to low water solubility and potential for hydrolysis and there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically it has not been demonstrated that the maximum concentration possible under the conditions of test was achieved and that undissolved test material was separated from the test media.

On this basis, the information requirement is not fulfilled.

Study design

The Substance is difficult to test due to the low water solubility. OECD TG 201 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 201. 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.

Appendix B: Reasons to request information required under Annex VIII of REACH

1. Long-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.). Long-term toxicity testing on fish must be considered (Section 9.1.3., Column 2) if the substance is poorly water soluble.

You have provided an OECD TG 203 study but no information on long-term toxicity on aquatic invertebrates for the Substance.

We have assessed this information and identified the following issue:

As described in section A.4, poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests does not give a true measure of toxicity for this type of substances and the long-term test is required.

As already explained under Section A.4, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

The examination of the information provided, as well as the selection of the requested test and the test design are addressed under section C.3.

2. Adsorption/ desorption screening

Adsorption/ desorption screening is an information requirement in Annex VIII to REACH (Section 9.3.1.).

You have provided an adaptation under Annex XI, Section 1.3 ('QSAR') with the following supporting information:

i. a Log Koc estimate based on the fragment method from KOWWIN (v2.00) (Kow method and MCI method).

We have assessed this information and, in addition to the deficiency described in the Appendix on reasons common to several requests, we have identified the following issue:

The prediction is not adequate due to low reliability

Under ECHA Guidance 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. ECHA Guidance R.6.1.5.3. specifies that, among others, the following condition must be met:

- reliable input parameters are used.

In your dossier for the EPIWin KOCWIN v2.00 using the LogKow method, you indicate that "*the calculated logKow used for this method is outside of the applicability domain of the QSAR model*".

As the input of the Koc model cannot be considered reliable (See also Appendix A.2), the Koc prediction is also considered unreliable.

On this basis, the information requirement is not fulfilled.

3. Simulation testing on ultimate degradation in surface water

Further degradation testing must be considered if the chemical safety assessment (CSA)

according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further degradation investigation (Annex I, Section 4; Annex XIII, Section 2.1), such as if the substance is a potential PBT/vPvB substance (ECHA Guidance R.11.4.). 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.* <60/70% 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),
- it meets the T criteria set in Annex XIII: NOEC or EC_{10} < 0.01 mg/L or classification as carc. 1A or 1B, muta. 1A or 1B, repro. 1A, 1B or 2, or STOT RE 1 or 2.

Your registration dossier provides the following:

- The Substance is not readily biodegradable (<10% degradation after 28 days in OECD TG 301B);

Furthermore, the information in your dossier is currently incomplete and therefore:

- it is not possible to conclude on the bioaccumulation potential of the Substance. While the information requirement on the partition coefficient n-octanol/water is not met due to inadequate reliability of the information provided (see Appendix A.2), the information available suggests that it is highly likely that the Substance has a log Kow above 4.5 and therefore a high potential for bioaccumulation. However, in the absence of the information requested under Appendix C.7, no conclusion can be reached;
- it is not possible to conclude on the toxicity of the Substance (see Appendices A.3, A.5 and C.1 to C.3 of this decision).

The information above indicates that the Substance is a potential PBT/vPvB substance.

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

The examination of the available information or adaptations, as well as the selection of the requested tests and the test design are addressed Appendix C.4.

4. Sediment simulation testing

Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

As already explained under Section B.3, the Substance is a potential PBT/vPvB substance. Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

The examination of the available information or adaptations, as well as the selection of the requested tests and the test design are addressed Appendix C.5.

5. Identification of degradation products

Further degradation testing must be considered if the chemical safety assessment (CSA)

according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

As already explained under Section B.3, the Substance is a potential PBT/vPvB substance. Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

The examination of the available information or adaptations, as well as the selection of the requested tests and the test design are addressed Appendix C.6.

6. Bioaccumulation in aquatic species

Bioaccumulation in aquatic species is required for the purpose of PBT/vPvB assessment (Annex I, Sections 0.6.1 and 4 to REACH).

This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further investigation on bioaccumulation in aquatic species (Annex I, Section 4; Annex XIII, Section 2.1), such as if the substance is a potential PBT/vPvB substance (ECHA Guidance R.11.4.).

As already explained under Section B.3, the Substance is a potential PBT/vPvB substance. Therefore, the chemical safety assessment (CSA) indicates the need for investigation on bioaccumulation in aquatic species.

The examination of the available information or adaptations, as well as the selection of the requested tests and the test design are addressed Appendix C.7.

Appendix C: Reasons to request information required under Annex IX of REACH

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

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is an information requirement under Annex IX to REACH (Annex 8.7.2., column 1). Annex IX, Section 8.7.2., column 2 provides that the decision on the need to perform a PNDT study on a second species at a tonnage level of 100 to 1000 tonnes per year should be based on the outcome of the PNDT study on a first species and all other relevant and available data.

You have provided a pre-natal developmental toxicity study with rabbits by the oral route ([redacted], 1988).

We have assessed this information and identified the following issue:

> A PNDT study on a second species is required if there is a concern for developmental toxicity based on the results from the PNDT study on a first species and other relevant data.
>
> You consider that no developmental toxicity was observed in the available study. In the high dose group of the available PNDT study, 3 rabbits out of 15 had a miscarriage. You consider this result as insignificant and you disregarded this effect. You also mentioned that there were no particular malformations in the foetuses observed. Therefore, you concluded that the Substance has no effects on reproduction and is not teratogenic.
>
> However, there is a concern based on information from a first species and taking all the available information into account as required in column 2 at Annex IX, section 8.7.2. Developmental toxicity was observed in one species in the available study (PNDT in rabbits, [redacted], 1988) at dose levels which were not markedly toxic to dams. More specifically, the NOAEL for developmental toxicity in this study has been set to 200 mg/kg, even though the effects at 200 mg/kg suggest developmental effects occurred, such as miscarriages observed in 3/15 (20%) and malformations (one foetus at 50 mg/kg bw /day showed aplasia of the head and at 200 mg/kg bw/day the foetus showed internal hydrocephalus.). No maternal toxicity was observed (such as reduction of body weight) that would explain the occurence of these effects.

As the condition of Annex IX, section 8.7.2., column 2 is fulfilled, a pre-natal developmental toxicity study in two species is an information requirement for your registration.

You have not provided an OECD TG 414 on a second species.

Based on the above, the information you provided does not fulfil the information requirement.

Study design

A PNDT study according to the OECD TG 414 study should be performed in the rat as the preferred species. The test in the first species was carried out by using a non-rodent species (rabbit). Therefore, a PNDT study in a second species must be performed in the rat as preferred rodent species. The study shall be performed with oral[3] administration of the Substance.

[3] ECHA Guidance R.7a, Section R.7.6.2.3.2.

2. Long-term toxicity testing on aquatic invertebrates

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

You have provided a Daphnia magna reproduction test (OECD TG 211), [redacted], 2013.

We have assessed this information and identified the following issues:

To fulfil the information requirement, a study must comply with the OECD TG 211 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) because the substance is difficult to test due to the low water solubility (as discussed above) and potential for hydrolysis (Article 13(3) of REACH). Therefore, the following specifications must be met:

Characterisation of exposure

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;
  in semi-static tests, if the concentration of the test material is not expected to remain within ± 20 % of the nominal concentration, then all test concentrations must be determined when freshly prepared and at the time of renewal on one occasion during each week of the test.

Additional requirements applicable to difficult to test substances

- As the test material is poorly water soluble, the maximum dissolved concentration that can be achieved in the specific test solution under the test conditions is determined;
- demonstration that the stock solution preparation method:
  - is of adequate quality (*e.g.* water solubility limit is reached when targeted), and
  - allows to produce reproducible stock solutions (*i.e.* acceptable variation between preparations);
- visual observations is not sufficient to demonstrate that the water solubility limit is reached;
- if the test material is tested at the saturation concentration, evidence must be provided that all reasonable efforts have been taken to achieve a saturation concentration, which include:
  4) an analytical method validation report demonstrating that the analytical method is appropriate, and
  5) information on the saturation concentrations of the test material in water and in the test solution, and
  6) the results of a preliminary experiment demonstrating that the test solution preparation method is adequate to maximize the concentration of the test material in solution;
- the efficacy of the separation method is assessed (*e.g.* by checking for the Tyndall effect or by any other appropriate means);
- a justification for, or validation of, the separation technique is provided;
- a justification must be provided if the concentration of the test chemical in the test solution cannot be analytically measured after the separation of non-dissolved test material (*i.e.* the dissolved concentration is below the limit of detection). The justification must explain why a lower detection limit could not be achieved;

Your registration dossier provides an OECD TG 211 showing the following:

Characterisation of exposure

- no analytical monitoring of exposure was conducted;

Additional requirements applicable to difficult to test substances

- The maximum dissolved concentration that can be achieved in the specific test solution under the test conditions was not determined;
- It was not demonstrated that the stock solution preparation method:
  - is of adequate quality (*i.e.* water solubility limit is reached when targeted), and
  - allows to produce reproducible stock solutions (*i.e.* acceptable variation between preparations);
- Visual observations was used to demonstrate that the water solubility limit is reached;
- You did not provide evidence that all reasonable efforts have been taken to achieve a saturation concentration, which include:
  - an analytical method validation report demonstrating that the analytical method is appropriate, and
  - information on the saturation concentrations of the test material in water and in the test solution, and
  - the results of a preliminary experiment demonstrating that the test solution preparation method is adequate to maximize the concentration of the test material in solution;
- The efficacy of the separation method by filtration has not been assessed;
- A justification for, or validation of, the filtration separation technique has not been provided;
- You have provided a justification that the concentration of the test chemical in the test solution cannot be analytically measured after the separation of non-dissolved test material because the dissolved concentration is below the limit of detection. You must explain why a lower detection limit could not be achieved.

Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically the exposure was not characterised;
- the Substance is difficult to test due to low water solubility and potential for hydrolysis and there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically it has not been demonstrated that the maximum concentration possible under the conditions of test was achieved and that undissolved test material was separated from the test media.

On this basis, the information requirement is not fulfilled.

Study design

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. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.5.

3. Long-term toxicity testing on fish

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

You have provided a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you derive RCRs <[redacted] for the uses

of the substance.

We have assessed this information and identified the following issue:

Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1. It must be understood as a trigger for providing further information on long-term toxicity to fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

Your adaptation is therefore rejected.

On this basis, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

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' under Appendix A.5.

4. Simulation testing on ultimate degradation in surface water

Simulation testing on ultimate degradation in surface water is an information requirement under Annex IX to REACH (Section 9.2.1.2.).

You have provided an adaptation under an adaptation under Annex IX, Section 9.2., Column 2 with the following justification: '*Simulation biodegradation tests in water and sediment are not proposed, since the test substance is highly insoluble in water and no relevant new findings are expected from such investigations*'.

We have assessed this information and identified the following issues:

A. Column 2 adaptation based in high insolubility

Under Section 9.2.1.2., Column 2 of Annex IX to REACH, the study may be omitted if the substance is highly insoluble in water. In this context, it must be demonstrated that it is technically not possible to conduct the study as a consequence of the low water solubility of the substance. The specific technical limitations of the OECD TG 309 must be respected, in particular:

- for the determination of biodegradation kinetics, the concentrations of the test substance must be below its water solubility, and
- the limit of quantification (LOQ) should be equal to or less than 10% of the applied concentration.

Considering the above, a simulation testing on ultimate degradation in surface water according to OECD TG 309 is considered technically feasible if the LOQ of a sensitive analytical method is at least ten times lower to the water solubility of the substance.

As explained under Appendix A.1, the information requirement on water solubility is not met. Furthermore, you have not provided information on the lowest achievable LOQ that can derived from a sensitive analytical method and a justification of why an adequate LOQ cannot be reasonably obtained.

The OECD TG 309 must be conducted at low test concentrations to ensure that the biodegradation kinetics obtained in the test reflect those e xpected in the environment. In this context low solubility in itself is not valid justification to omit this information requirement. Taken together, the information from your dossier does not demonstrated convincingly that an OECD TG 309 study is not technically feasible (also considering the possibility to lower the LOQ of the analytical method by using a radiolabelled test material). Therefore, your adaptation is rejected.

B. The CSA indicates a need to investigate further the degradation of the substance

Under Section 9.2., Column 2 of Annex IX to REACH, the study may be omitted if the chemical safety assessment (CSA) does not indicate the need for further biotic degradation testing. The CSA does indicate such need (Annex I, Section 4; Annex XIII, Section 2.1) if, for instance, the substance is a potential PBT/vPvB substance (ECHA Guidance R.11.4).

As already explained under Section B.3, the Substance is a potential PBT/vPvB substance. Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

As already explained under Appendix B.3, you have not demonstrated that the CSA does not indicate the need for further biotic degradation testing and your adaption is rejected.

On this basis, the information requirement is not fulfilled.

Study design

Simulation degradation studies must include two types of investigations (ECHA Guidance 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.

You must perform the test, by following the pelagic test option with natural surface water containing approximately 15 mg dw/L of suspended solids (acceptable concentration between 10 and 20 mg dw/L) (ECHA Guidance R.11.4.1.1.3.).

The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (ECHA Guidance R.16, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 309.

As specified in ECHA Guidance R.7.9.4.1., the organic carbon (OC) concentration in surface water simulation tests is typically 2 to 3 orders of magnitude higher than the test substance concentration and the formation of non-extractable residues (NERs) may be significant in surface water tests. Therefore, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents. 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) (ECHA Guidance 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.

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 309; ECHA Guidance R.11.4.1.).

5. Sediment simulation testing

Sediment simulation testing is an information requirement under Annex IX to REACH (Section 9.2.1.4.) for substances with a high potential for adsorption to sediment.

The Substance is likely to have a low water solubility, a high partition coefficient and high adsorption coefficient and therefore is condiered to have a high potential for adsorption to sediment.

You have provided an adaptation under an adaptation under Annex IX, Section 9.2., Column 2 with the following justification: '*Simulation biodegradation tests in water and sediment are not proposed, since the test substance is highly insoluble in water and no relevant new findings are expected from such investigations*'.

We have assessed this information and identified the following issue:

A. Column 2 adaptation

Under Section 9.2.1.4., Column 2 of Annex IX to REACH, the study may be omitted if the substance is readily biodegradable or if direct and indirect exposure of sediment is unlikely.

Section 9.2.1.4., Column 2 of Annex IX to REACH does not foresee the possibility to omit the test based on low water solubility. Therefore, your adaptation is rejected.

B. The CSA indicates a need to investigate further the degradation of the substance

Under Section 9.2., Column 2 of Annex IX to REACH, the study may be omitted if the chemical safety assessment (CSA) does not indicate the need for further biotic degradation testing. The CSA does indicate such need (Annex I, Section 4; Annex XIII, Section 2.1) if, for instance, the substance is a potential PBT/vPvB substance (ECHA Guidance R.11.4).

As already explained under Section B.3, the Substance is a potential PBT/vPvB substance. Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

As already explained under Appendix B.3, you have not demonstrated that the CSA does not indicate the need for further biotic degradation testing and your adaption is rejected.

On this basis, the information requirement is not fulfilled.

Study design

Simulation degradation studies must include two types of investigations (ECHA Guidance 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.

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.

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

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 (ECHA Guidance 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) (ECHA Guidance 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.

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; ECHA Guidance R.11.4.1.).

6. Identification of degradation products

Identification of degradation products is an information requirement under Annex IX to REACH (Section 9.2.3.).

Under section 5.1.2 of your technical dossier you state the following:

- "*in general organophosphites, such as the* [Substance], *are known to be hydrolytically unstable*";
- "*the hydrolysis of the phosphite group would result in '2,4-di-tert-butylphenol' as metabolite*";
- "[However] *due to the steric effects of the tert-butyl grop in both position 2 and 4 the hydrolysis is significantly reduced and the test substance will hydrolyse only slowly*";
- "*Due to the extensive adsorption of the test item combined with the low water solubility it was impossible to analyze the hydrolysis* [in a study according to OECD TG 111]".

You have not provided any other information on the identification of degradation products for the Substance.

We have assessed this information and identified the following issues:

A. Annex XIII to REACH specifies that the information used for the purpose of assessment of the PBT/vPvB properties must be based on data obtained under relevant conditions.

   You state that the chemical structure of the substance indicates a potential for hydrolysis. However, based on an experimental study according to OECD TG 111, you

were unable to provide an experimental demonstration that significant hydrolysis occurs.

Therefore, you have not demonstrated that hydrolysis products are likely to be formed under environmentally relevant conditions.

B. ECHA Guidance R.11.4.1.1.2. specifies that all relevant degradation pathways (biotic, abiotic, aerobic, anaerobic conditions) need to be considered with regard to the relevant route of exposure before concluding on persistence.

As explained under issue A., the available information from your dossier does not demonstrate that the Substance is likely to be subject to significant hydrolysis under relevant conditions. You have not provided any other information on the formation of degradation products.

Therefore, as it cannot be excluded that transformation products may be formed following other degradation processes (e.g. biotic degradation), your technical dossier fails to consider all relevant degradations pathways.

On this basis, the information requirement is not fulfilled.

Study design

Regarding the selection of appropriate and suitable test method(s), the method(s) will have to be substance-specific. Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported, when analytically possible. In addition, degradation half-life, log K_{ow} and potential toxicity of the transformation/degradation may need to be investigated. You may obtain this information from the degradation studies requested in Appendices C.4 and C.5 or by some other measure. If any other method is used for the identification of the transformation/degradation products, you must provide a scientifically valid justification for the chosen method.

To determine the degradation rate of the Substance, the requested study according to OECD TG 309 (Appendix C.4) must be conducted at 12°C and at a test concentration < 100 µg/L. 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, *e.g.* 20°C) and at higher application rate (*i.e.* > 100 µg/L).

Alternatively, to determine the degradation rate of the Substance, the requested study according to OECD TG 308 (Appendix C.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

Bioaccumulation in aquatic species is a standard information requirement under Annex IX to REACH (Section 9.3.2.).

You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.2. of REACH (weight of evidence).

In support of your adaptation, you have provided the following sources of information:

i. A QSAR estimate of BCF using BCFBAF v3.01 (EPI Suite v4.11).
ii. A QSAR estimate of BCF using CATALOGIC 5.11.19.
iii. A QSAR estimate of BCF using T.E.S.T. v4.2.1.
iv. Indicators for low likelihood of high bioaccumulation potential

Based on the presented sources of information, you argue that the available data gives sufficient information to conlude '*that the test substance does not significantly accumulate in organisms*'.

Annex XI, Section 1.2 states that there may be sufficient weight of evidence weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study.

Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence adaptation.

You have not included a justification for your weight of evidence adaptation, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Irrespective of the above mentioned deficiencies on the documentation, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided sources of information.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.3.2. at Annex IX includes similar information that is produced by the OECD TG 305, which include the following key parameters:

- the uptake rate constant (k_1) and loss rate constants including the depuration rate constant (k_2), and/or
- the steady-state bioconcentration factor (BCF_{SS}), and/or
- the kinetic bioconcentration factor (BCF_K), and/or
- the biomagnification factor (BMF).

The sources of information (i) to (v) provide relevant information on bioaccumulation potential, but have the following deficiencies affecting their reliability:

A. Lack of or inadequate documentation of the prediction (QPRF)

As explained in the Appendix on reasons common to several requests, you did not submit documentation of the QSAR predictions you rely on.

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

Under ECHA Guidance R.6.1.5.3., a substance must fall within the applicability domain specified by the model developer.

- Concerning the QSAR estimate of BCF using BCFBAF v3.01 (EPI Suite v4.11)

  The log Kow of the substance is 10.9, whereas the maximum logKow is 9 for the substances in the training set of the Arnot & Gobas BCF model of the BCFBAF module in EPISuite. Therefore, in your dossier you state "*Log Kow is outside of range of training set. Therefore, the estimate may be less accurate*."

  The substance is outside the applicability domain of the the Arnot & Gobas BCF model of the BCFBAF module in EPISuite.

- Concerning the QSAR estimate of BCF using CATALOGIC 5.11.19

  Your QPRF contains the following information:
  "*ii. Structural fragment domain:*
  The following ACF are identified:
  Fragments in correctly predicted training chemicals – 48.39%
  Fragments in non-correctly predicted training chemicals – 25.81%
  Fragments not present in the training chemicals – 25.81%
  CONCLUSION:
  The chemical is out of the interpolation structural space"

  As indicated in your QPRF, the substance is outside the applicability domain of the model. In particular, a severe shortcoming is the presence of non-correctly predicted fragments in the structure suggest that the model's prediction may not be accurate for the Substance.

C. The prediction is not adequate due to low reliability

Under ECHA Guidance 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. ECHA Guidance R.6.1.5.3. specifies that, among others, the following condition must be met:

- reliable input parameters are used.

- Concerning the QSAR estimate of BCF using BCFBAF v3.01 (EPI Suite v4.11)

  Both regression (Meylan) and Arnot & Gobas models of the BCFBAF module in EPISuite use Kow as input predicted using the EPIWin KOCWIN v2.00 LogKow method.

  In your dossier for the EPIWin KOCWIN v2.00 LogKow method you indicate that "*the calculated logKow used for this method is outside of the applicability domain of the QSAR model*".

  A calculated logKow is used as input for the regression (Meylan) and Arnot & Gobas models of the BCFBAF module in EPISuite method. As the input cannot be considered reliable (see Appendix A.2.), then the output is also unreliable, i.e. the BCF predictions.

- Concerning the QSAR estimate of BCF using T.E.S.T. v4.2.1.

  In your QPRF, the BCF predictions from T.E.S.T. consensus model are obtained by combining the predictions of its sub-models:

Hierarchical clustering	*Not in domain*
FDA method	*In domain*
Single model	*Not in domain*
Group contribution	*Not in domain*
Nearest neighbour	*In domain*
Consensus	*In domain*

  The consensus model only considers predictions within domain, i.w. the FDA method and the nearest neighbour models.

  Furthermore, the following confidence in the estimated BCF is provided in your QPRF:

  FDA: high confidence in external test set, low confidence in the training set
  Nearest neighbour: low confidence in the external test set, high confidence in the training set.

  The T.E.S.T consensus model uses as input the predictions from the FDA method and nearest neighbour models, which are identified with low confidence in either the training or external test set. For this reason, the overall Consensus prediction is considered not reliable due to the low reliability of the input parameters.

D. Available evidence do not support a low potential to cross biological membranes

Under Section 9.3.2., Column 2, first indent, Annex IX to REACH, the study may be omitted if the Substance is unlikely to cross biological membranes. ECHA Guidance 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 (ECHA Guidance 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).

The Indicators for low likelihood of high bioaccumulation potential you submitted in your registration dossier provides physico-chemical indicators which you consider supportive of hindered uptake:

- a QSAR estimate of log Kow 10.9, and
- a QSAR estimate of D_{max} = 20.2 Å by CATALOGIC v5.11.19.

Available information on the Substance do not support that the Substance is unlikely to cross biological membranes because effects supporting systemic exposure were observed in repeated-dose toxicity, reproductive toxicity and developmental toxicity studies. Therefore your argument that the substance is of low potential for bioaccumulation is not supported.

On this basis, the reliability of all the sources of information you submitted is affected by significant deficiencies and therefore provide limited support to your weight of evidence adaptation.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 305 study because none of the supporting information (i) to (iv) is reliable. As a result, your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

Bioaccumulation in fish: aqueous and dietary exposure (Method EU C.13 / OECD TG 305) is the preferred test to investigate bioaccumulation (ECHA Guidance 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 substance 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.

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

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).

Appendix D: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. 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[4].

B. 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[5].

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

Appendix E: General recommendations when conducting and reporting new tests for REACH purposes

A. Strategy for the PBT/vPvB assessment

You are advised to consult ECHA Guidance R.7b (Section R.7.9.), R.7c (Section 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.

Appendix F: 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 12 May 2020.

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 G: List of references - ECHA Guidance[6] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[7]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[7]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

[6] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[7] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

OECD Guidance documents[8]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

[8] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix H: Addressees of this decision and their corresponding information requirements

You must provide the information requested in this decision for all REACH Annexes applicable to you.

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