~~Confidential~~

Helsinki, 08 June 2022

Addressees
Registrant(s) of JS_DYBP_1068-27-5 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
16/06/2021

Registered substance subject to this decision ("the Substance")
Substance name: Di-tert-butyl 1,1,4,4-tetramethylbut-2-yn-1,4-ylene diperoxide
EC number: 213-944-5

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 ***14 September 2026***.

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. 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

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

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

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

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

2. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats

3. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD TG 203)

4. Simulation testing on ultimate degradation in surface water (triggered by Annex VIII, Section 9.2.) Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.

5. Soil simulation testing (triggered by Annex VIII, Section 9.2.) Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.

6. Sediment simulation testing (triggered by Annex VIII, Section 9.2.) Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.

7. Identification of degradation products (triggered by Annex VIII, Section 9.2; test method: using an appropriate test method

8. Bioaccumulation in aquatic species (triggered by Annex I, sections 0.6.1. and 4.; Annex XIII, Section 2.1.; test method: OECD TG 305, aqueous exposure)

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

- Appendix entitled "Reasons common to several requests";
- Appendices entitled "Reasons to request information required under Annexes VII to VIII 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 Annexes VII and VIII to REACH, for registration at 10-100 tpa.

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 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 Mike Rasenberg, 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 read-across approach under Annex XI, Section 1.5.

i. Assessment of the Grouping of substances and read-across approach under Annex XI, Section 1.5.

You seek to adapt the following standard information requirements by applying a read-across approach in accordance with Annex XI, Section 1.5:

- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

ECHA has considered the scientific and regulatory validity of your read-across approach in general before assessing the specific standard information requirements in the following appendices.

Grouping of substances and read-across approach

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

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6. and related documents[2,3].

A. Predictions for toxicological properties

You have provided a read-across justification document in IUCLID Section 13.

You read-across between the structurally similar substances, di-tert-butyl 1,1,4,4-tetramethyltetramethylene diperoxide, EC No. 201-128-1 (CAS No. 78-63-7) as source substance and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties: *"This read-across is based on the hypothesis that source and target substances exhibit the same toxicological profile based on common underlying mechanisms due to same functional groups and degradation products. This prediction is supported by physicochemical and toxicological data on the substances".*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

[2] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)

[3] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: https://doi.org/10.2823/794394

ECHA notes the following shortcoming with regards to predictions of toxicological properties.

Supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*" (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.). The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include bridging studies to compare properties of the Substance and source substance.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

In order to support your claim that the Substance and source substance have similar properties for the endpoints under consideration in the read-across approach, you refer to:

- Structural similarity with the only difference being that the Substance contains a triple bond between the 3rd and 4th carbon atom of the hydrocarbon chain;
- Information from acute oral and dermal studies, skin and eye irritation studies, skin sensitisation studies and *in vitro* genetic toxicity studies for the Substance and source substance indicating similar properties for the target and the source substance;
- QSAR Toolbox evaluation for the presence or absence of relevant structural alerts indicating similarity in the comparison of the QSAR Toolbox (version 3.3.5.17) profiling schemes.

Furthermore, to support the similarity in the expected degradation of the source and target substances to a common and similar hydrolysis products, you have provided information on the hydrolysis of the Substance and source substance. You indicate that the hydrolysis half-life for the Substance is 9 days (at 20ºC) and for the source substance 4.4 hours (at 20ºC). You state that "*In regards to the target substance, the hydrolysis rate was shown to be rather slow, absorption in the gastro intestinal tract (GIT) will mainly be limited to the parent compound. This is probably the main difference to the source substance which hydrolyses within a few hours and which hydrolysis products may become important earlier in regards to bioavailability*."

As you also indicate, there is a structural difference between the Substance and the source substance, with the Substance containing an alkyne functional group in the hydrocarbon chain, which is not present in the source substance. Furthermore, there is a potential exposure to different compounds after oral administration of the Substance and source substance due to:

- longer hydrolysis half-life for the Substance (9 days at 20ºC) compared to the source substance (4.4 h at 20ºC) with the test organism expected to be mainly exposed to the parent compound in the case of the Substance, whereas the test organism will mainly be exposed to the hydrolysis products in the case of the source substance;

- presence of parrafin oil as an additive in the Substance (ca. [redacted]%) but not part of the test substance composition used for the source studies.

Therefore, the impact of the structural difference and the potential exposure to different compounds as a result of the differences in hydrolytical stability of the Substance and source substance needs to be assessed to ensure that a reliable prediction can be made. However, you have not considered the exposure to the different compounds resulting from exposure to the Substance and to the source substance.

Furthermore, as explained below, the supporting information does not include relevant, reliable and adequate information for the Substance and of the source substance to support your read-across hypothesis.

Firstly, while the information on acute toxicity, irritation, skin sensitisation and in vitro genotoxicity of the substances may provide support that the substances have similarities for these toxicological properties, these studies do not inform on the repeated dose toxicity, sexual function, fertility and developmental properties of the target and source substances. Therefore, this data set does not provide relevant information for the Substance and for the source substance to support your read-across hypothesis.

Secondly, the information from the physico-chemical properties and QSAR predictions may indicate that the structural differences between the Substance and the source substance do not influence the reactivity and behaviour of the substances. However, due to the complexity of the systemic interactions as well as the large number of targets/mechanisms associated with repeated dose and reproductive (including developmental) toxicity, the information from the computational tools needs to be supported by further data.

Thus, the data set reported in the justification document and in the technical dossier does not include relevant, reliable and adequate information for the Substance and of the source substance to support your read-across hypothesis.

In the absence of such information, you have not established that the Substance and the source substance are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

B. Conclusions on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substance. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

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

1. 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.).

You have provided a key study in your dossier:

i. Bacterial reverse mutation test (performed according to OECD TG 471, GLP, 1983).

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

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[4] (1997). One of the key parameters of this test guideline includes that the test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

The reported data for the study you have provided did not include results for the required fifth strain, *S. typhimurium* TA 102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) as it was conducted with the following strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538.

The information provided does not cover one of the key parameters required by OECD TG 471.

Therefore, 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.

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

2. Short-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.).

Information provided

You have provided the following information:

i. a study according to OECD TG 202 and EU Method C.2, with the Substance.

Assessment of the information provided

We have assessed this information and identified the following issues:

The provided study does not meet the information requirement

To fulfil the information requirement, a study must comply with OECD TG 202 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:

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

Characterisation of exposure

a) the concentrations of the test material are measured at least at the highest and lowest test concentration, at the beginning and end of the test;
b) the effect values can only be based on nominal or measured initial concentration if the concentration of the test material has been satisfactorily maintained within 20 % of the nominal or measured initial concentration throughout the test (see also ECHA Guidance R.7b, Section R.7.8.4.1).

Additional requirements applicable to difficult to test substances regarding:

c) demonstration that the stock solution preparation method:
   1) allows to produce reproducible stock solutions (*i.e.* acceptable variation between preparations);
d) if water-accommodated fractions (WAFs) are used, they must be prepared separately for each dose level;
e) if water-accommodated fractions (WAFs) are used, a preliminary study must be conducted to determine that saturation has been achieved;
f) the efficacy of the separation method is assessed (*e.g.* by checking for the Tyndall effect or by any other appropriate means).

Your registration dossier provides an OECD TG 202 showing the following:

Characterisation of exposure

a) the concentration of the test material was determined only at the highest test concentration;
b) the concentration of the test material was not maintained within 20% of the initial measured concentration (i.e. decreased from 5.31 mg/L to 0.38 mg/L at the highest test concentration). You have expressed the effect values based on initial measured concentration.

Additional requirements applicable to difficult to test substances regarding:

c) You have prepared a WAF solution applying 48h stirring and phase separation and you have not reported the analytical measurements confirming reproducibility;
d) you have prepared all dose levels, except the highest dose, by WAF dilution;
e) you have not provided a preliminary study demonstrating that maximum saturation has been achieved;
f) you have not validated the separation method used, confirming removal of undissolved particles (e.g. Tyndall effect).

Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, in the absence of analytical monitoring at the lowest test concentrations, you have not demonstrated that the organisms were actually exposed to the test material throughout the test in the lower doses (i.e. 1:2, 1:4, 1:8, 1:16 and 1:32 dilutions of the WAF). Additionally, the concentration at the highest dose was not stable but you report the effect value based on initial measured concentration.
- the Substance is difficult to test due to high reactivity and adsorption potential and there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, in the absence of a preliminary study and validation of the separation technique, you have not demonstrated that the maximum saturation

concentration was achieved in the WAF test solution and that the reported observations (i.e. daphnids floating at the surface in all dilutions) are not resulting from the presence of undissolved test material.

Therefore, the requirements of OECD TG 202 are not met. On this basis, the information requirement is not fulfilled.

Study design and test specifications

The Substance is difficult to test due to the adsorptive properties: Log Kow 6.71 and subjectivity to transformation (peroxide). The OECD TG 202 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 202. 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.

In the comments to the draft decision, you agree to perform the requested study.
Your comments related to tiered testing are addressed in Appendix E of this decision.

3. Growth inhibition study aquatic plants

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

Information provided

You have provided the following information:

i. a study according to OECD TG 201 and EEC (1992): L383 A/179

Assessment of the information provided

We have assessed this information and identified the following issues:

The provided study does not meet the information requirement

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:

Characterisation of exposure

a) the test media prepared specifically for analysis of exposure concentrations during the test is treated identically to those used for testing (*i.e.* inoculated with algae and incubated under identical conditions);
b) the concentrations of the test material are measured at least at the beginning and end of the test:
   1) at the highest, and
   2) at the lowest test concentration, and

3) at a concentration around the expected EC_{50}.
4) for volatile, unstable or strongly adsorbing test substances, additional samplings for analysis at 24 hour intervals is required.

c) the results can be based on nominal or measured initial concentration only if the concentration of the test material has been maintained within ±20 % of the nominal or measured initial concentration throughout the test.
d) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

Validity criteria

e) exponential growth in the control cultures is observed over the entire duration of the test;
f) at least 16-fold increase in biomass is observed in the control cultures by the end of the test;
g) the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%;
h) the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures is ≤ 7% in tests with *Pseudokirchneriella subcapitata*.

Additional requirements applicable to difficult to test substances regarding:

i) demonstration that the stock solution preparation method:
   1) allows to produce reproducible stock solutions (*i.e.* acceptable variation between preparations);
j) if water-accommodated fractions (WAFs) are used, they must be prepared separately for each dose level;
k) if water-accommodated fractions (WAFs) are used, a preliminary study must be conducted to determine that saturation has been achieved.
l) the efficacy of the separation method is assessed (*e.g.* by checking for the Tyndall effect or by any other appropriate means).

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

Characterisation of exposure

a) the reported analysis of exposure concentrations was determined in the undiluted WAF only (i.e. not inoculated with algae);
b) the concentration of the test material was determined at the highest concentration only;
c) The concentrations of the test material in WAF were 3.76 mg/L at the beginning of the test and below 0.3 mg/L after 24 hours and thus not within ± 20 % of nominal or measured initial concentration throughout the test. You have expressed the effect values based on initial measured concentration.
d) tabulated data on the algal biomass determined daily for each treatment group and control are not reported;

Validity criteria

e) you have claimed that validity criteria were fulfilled and that a 124-fold increase was observed in the controls, but you have not reported coefficient of variations allowing the assessment of all validity criteria specified in OECD TG 201

Additional requirements applicable to difficult to test substances regarding:

f) You have prepared a WAF solution applying 48h stirring and phase separation and you

have not reported the analytical measurements confirming reproducibility;
g) you have prepared all dose levels, except the highest dose, by WAF dilution;
h) you have not provided a preliminary study demonstrating that maximum saturation has been achieved;
i) you have not validated the separation method used, confirming removal of undissolved particles (e.g. Tyndall effect).

Based on the above,

- in the absence of tabulated data regarding cell growth, it is not possible to conduct an independent assessment of the study validity.
- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, in the absence of analytical monitoring at the lowest test concentrations, you have not demonstrated that the organism were actually exposed to the test material throughout the test in the lower doses (i.e. 1:2, 1:4, 1:8, 1:16 and 1:32 dilutions of the WAF). Additionally, the concentration at the highest dose was not stable but you report the effect values based on initial measured concentration.
- the Substance is difficult to test due to high reactivity and adsorption potential and there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, in the absence of a preliminary study and validation of the separation technique, you have not demonstrated that the maximum saturation concentration was achieved in the WAF test solution and that undissolved particles were removed.

Therefore, the requirements of the OECD TG 201 are not met.

In the comments to the draft decision, you do not agree to perform the requested study. You indicate the following:

”As the green algae is not the most sensitive species, the performance of a new study with algae is not considered as scientifically justified. A new study would not change the assessment (C+L and hazard assessment of the substance). The mentioned shortcomings of the study (only one WAF and subsequent dilution) mentioned by ECHA are of no relevance as no effects were observed in the highest dose and only a limit test with one WAF would be needed to cover adequately the endpoint”

Finally, you mention that additional data from the original report will be provided.

ECHA has assessed the information provided and identified the following issues:

Firstly, you do not address any of the issues of the study provided in your dossier identified above (points a to i) and you do not ellaborate on the issues that you intend to address with the additional information available in the original report. In particular, regarding the information listed above under point g) you indicate that the issue raised by ECHA is not relevant since no effects were observed in the highest dose and only a limit test with one WAF would be needed to cover adequately the endpoint. However, as indicated above, you did not demonstrate that at the highest dose tested the maximum saturation was achieved, for the reasons explained above (i.e. lack of preliminary study and validation of the separation technique). Moreover, the study shortcoming related to the assessmernt of study validity, as listed above, remains. Therefore, a limit test performed in the same conditions as the study assessed above would not be acceptable to conclude on this information requirement. On this basis, the information in your comments do not address the deficiencies on the study as pointed out above.

Secondly, you do not indicate in your comments any legal basis for an adaptation of the information requirement other than referring to a new study being considered scientifically not justified. A registrant may only adapt this information requirement based on the general rules set out in Annex XI or based on the conditions set out in An. VII, Column 2, Section 9.1.2. Your comments refer to the lack of effects, the most sensitive species and the impact of a new study on hazard assessment and C&L hence they do not refer to an acceptable adaptation of this information requirement. Furthermore, currently your dossier does not contain any acceptable study covering the aquatic toxicity of the Substance (see Sections A.2-3 and B.2 in this decision). Therefore it is not yet possible to conclude on the aquatic toxicity of the Substance, the identity of the most sensitive species or the need for classification.

In your comments, you stated that you will provide information contained in the original dossier in an update of your registration dossier. As stated above, you do not define the content of the information nor the issues it would address hence the information in your comments is not sufficient for ECHA to make an assessment. ECHA will assess your dossier update after the expiry deadline set in this decision.

Your comments related to tiered testing are addressed in Appendix E of this decision.

On this basis, the information requirement is not fulfilled.

Study design and test specifications

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 Appendix A.2.

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

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

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII to REACH.

For the information on short-term repeated dose toxicity, you have sought to adapt the standard information requirement according to Annex XI, Section 1.5.

You have provided the following information, relevant for this endpoint:

i. 90-day repeated dose toxicity study in rats according to the OECD TG 408, GLP, performed with the source substance ([redacted] 2014a).

As explained in the Appendix on Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected.

Therefore, the information requirement is not fulfilled.

Information on study design

When there is no information available neither for the 28-day repeated dose toxicity endpoint (EU B.7, OECD TG 407) nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1[5]

Therefore, a study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral administration of the Substance.

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

2. Screening for reproductive/developmental toxicity

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

For the information on reproductive toxicity, you have sought to adapt the standard information requirement according to Annex XI, section 1.5.

You have provided the following information, relevant for this endpoint:

i. Prenatal developmental toxicity study in rats according to OECD TG 414, GLP, performed with the source substance ([redacted] 2014b).

As explained in the Appendix on Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected.

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

Therefore, the information requirement is not fulfilled.

Information on study design

When there is no information available neither for the 28-day repeated dose toxicity endpoint (EU B.7, OECD TG 407) as explained above, nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1[6]

Therefore, a study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral administration of the Substance.

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

3. Short-term toxicity testing on fish

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

You have provided the following information:

i. a study according to OECD TG 203, with the Substance.

We have assessed this information and identified the following issues:

The provided study does not meet the information requirement

To fulfil the information requirement, a study must comply with OECD TG 203 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:

Requirements applicable to difficult to test substances regarding:

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

Your registration dossier provides an OECD TG 203 showing the following:

Requirements applicable to difficult to test substances regarding:

a) you have not provided a preliminary study demonstrating that maximum saturation has been achieved;
b) you have used filtration as separation technique and provided no justification.

Based on the above,

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

- the Substance is difficult to test due to high reactivity and adsorption potential and there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, in the absence of a preliminary study and a justification for the separation technique used, you have not demonstrated that maximum saturation concentration was achieved in the reported limit study. On this basis, you have not demonstrated that the Substance is not toxic to the organisms.

Therefore, the requirements of the OECD TG 203 are not met.

In the comments to the draft decision, you do not agree to perform the requested study.

You indicate that "the test solution was stirred for at least 24 hours to allow the test substance to dissolve as much as possible and the undissolved particles were removed by filtration. As no mortality or sublethal effects were observed in the study, the registrants do not agree to perform a new study due to animal welfare reasons. No further findings from a new study are expected, therefore, the performance of an animal study is considered scientifically unjustified. A new study would not change the assessment (C+L and hazard assessment of the substance). The mentioned shortcomings of the study (only one WAF and subsequent dilution) mentioned by ECHA are of no relevance as no effects were observed in the highest dose and only a limit test with one WAF would be needed to cover adequately the endpoint"

ECHA has assessed the information provided and identified the following issues:

Firstly, you repeat the information in you dossier regarding test solution preparation already addressed in shortcomings a) and b) of the study, as listed above. Furthermore, you refer to additional issues not brought up by ECHA (e.g. regarding WAF preparation). However, in your comments on the identified sample preparation shortcomings you have not provided any new scientific information that could address the deficiencies of the study provided as mentioned above.

Secondly, you do not indicate in your comments any legal basis for an adaptation of the information requirement other than referring to a new study being considered scientifically not justified. A registrant may only adapt this information requirement based on the general rules set out in Annex XI or based on the conditions set out in An. VIII, Column 2, Section 9.1.3. Your comments related to the lack of effects and the impact of a new study on hazard assessment and classification and labelling hence they do not refer to an acceptable adaptation of this information requirement. Furthermore, currently your dossier does not contain any acceptable study covering the aquatic toxicity of the Substance (see Sections A.2-3 and B.2 in this decision). Finally, you refer to animal welfare reasons in your comments however, minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI. Hence it is not yet possible to conclude on the aquatic toxicity of the Substance or the need for classification.

Your comments related to tiered testing are addressed in Appendix E of this decision.

On this basis, the information requirement is not fulfilled.

Study design and test specifications

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

4. 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 (Guidance on IRs and CSA, Section 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% degradation in an OECD TG 301D study), and
- 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).

Information provided

Your registration dossier provides the following:

- The Substance is not readily biodegradable (4% degradation after 28 days and 0% degradation after extended period of 140 days in OECD TG 301 D);
- The Substance has a high potential to partition to lipid storage (Log K_{ow} of 6.71 based on OECD TG 117);

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

- it is not possible to conclude on the bioaccumulation potential of the Substance (see Appendix B.8 of this decision), and
- it is not possible to conclude on the toxicity of the Substance see Appendices A.1 to A.3, B.1 and B.2 of this decision).

Under section 2.3 of your IUCLID dossier and section 8 of your CSR of your technical dossier ('PBT assessment'), you conclude that the Substance is not P/vP nor B/vB. In support of your conclusion you provide the following additional information: the Substance has a hydrolysis half-life of 9 days at pH 7 and the corresponding hydrolysis product is tert-butanol (CAS 75-65-0). Based on the inherent biodegradability and low Log Kow (Log Kow = 0.32) of the hydrolysis product, you conclude that the Substance does not meet P/vP nor B/vB criteria.

Annex XIII, Section 3.2 lists the information considered in the assessment of P/vP properties when screening information indicates that the substance may have PBT/ vPvB properties. Annex XIII, Section 3.2.1 (a-c) states that the results (i.e. degradation half-life) from water, soil and sediment simulation studies must be used to compare against the P/vP criteria stipulated in Annex XIII, Sections 1.1.1 and 1.2.1 (e.g. substance fulfils the P criteria if degradation half-life >40 days in fresh or estuarine water). Furthermore, ECHA Guidance R.11.4.1.1.1 states that concern for P/vP cannot be removed by significant and substantial loss of the parent substance by hydrolysis alone, but additional evidence is also needed to demonstrate rapid hydrolysis across all relevant environmental compartments (including marine water, estuarine water, sediment and soil). In addition, as hydrolysis is only primary degradation, careful consideration needs to be given also to the potential formation of stable degradation products with PBT/vPvB properties.

Additionally, ECHA Guidance R.7.10.3.4 consider hydrolysis as fast when hydrolysis half-life, at environmentally relevant pH values (4-9) and temperature, is less than 12 hours.
In your dossier, you have not provided simulation studies with the Substance under relevant environmental conditions.

In your PBT assessment of the Substance you concluded that: "The test item has a hydrolysis half-life of 9 days at pH 7. The degradation product detected is tert-butanol (CAS 75-65-0). This degradation product is one of the starting materials for the manufacturing of the test item. The degradation product is inherently biodegradable under environmental conditions and is hydrolytically stable. Based on this information, the test item is considered not to be P or vP substance."

As explained above, the Substance is potentially P/vP based on screening information, and in the absence of simulation studies under relevant environmental conditions, it is currently not possible to conclude on P/vP criteria.

Your conclusion that the Substance is not P/vP based on hydrolysis half-life is not valid because only half-life values derived from simulation studies can be used to compare against persistence criteria of Annex XIII. Furthermore, in concluding on the P criteria in your PBT assessment, you have focused only on the hydrolysis of the parent Substance. The reported hydrolysis half-life of 9 days cannot be considered as fast (significant and substantial) hydrolysis and hence it does not contribute to the conclusion on P/vP nor B/vB properties. Additionally, you have not considered other potential degradation products or impurities in you PBT assessment.

Therefore, you have not demonstrated that the CSA does not indicate the need for further biotic degradation testing and further degradation testing is required.

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

Based on the above, the available 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.

Study design and test specifications

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.

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) (Guidance on IRs and CSA, Section R.11.4.1.1.3.).

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 309.

As specified in Guidance on IRs and CSA, Section 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 material 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) (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.

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; Guidance on IRs and CSA, Section R.11.4.1.).

In the comments to the draft decision you indicate that "the simulation test on ultimate degradation in surface water is not the most appropriate compartment to start with. The registered substance has very high partitioning coefficient (logKow = 6.71), which means that the substance has high potential to adsorb, therefore, the ultimate degradation study in water is not considered to be the most appropriate study to start assessing the P/vP criterion. Some preliminary testing to determine the hydrolysis and adsorption properties of the registered substance will have to be done before going into the simulation testing. The registrant asks the Authorities to take this into account when setting the deadline. The read-across substance (CAS 78-63-7) has shown in additional hydrolysis tests that the disappearance of the parent substance from the system is not due to hydrolysis but due to adsorption. Additionally, a series of biodegradation studies (OECD 303A, 302A and closed bottle test) showed that the read-across substance is removed from the sewage treatment plant and no substance is released to any surface water or via sludge to the environment. The use profile for both substances (uses only in industrial setting) support the obtained information and show that there is none to low chance for exposure of the water compartment to the source substance. The same behaviour is expected and seen for the registered substance."

ECHA has assessed the information and identified the following issues:

You claim that water is not the most relevant compartment to conclude on P/vP and you base your reasoning on the Substance adsorption and distribution. You further support your arguments with information on an analogue substance (CAS 78-63-7), to indicate unlikelihood of distribution to the water compartment.

A. Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide a justification for the read-across including a hypothesis, explanation of the rationale for the prediction of properties and robust study summary(ies) of the study(ies) on the source substance(s) (Guidance on IRs and CSA, Section R.6.2.6.1.).

You have provided only overall statements regarding degradation and distribution in sludge of an other substance than the Substance. However, you have not provided documentation as to why this information is relevant for the Substance.

In the absence of such documentation, the properties of the Substance cannot be reliably predicted from the data on the source substance(s) hence you have not demonstrated how the data on the analogue is relevant to assess the Substance's distribution.

B. As specified in Appendix D of this decision you may decide on the sequence of simulation degradation testing considering the intrinsic properties of the Substance, and its identified uses and release patterns.

Regarding surface water simulation study, the aquatic compartment is considered to be a relevant environmental compartment by default because it receives significant amount of emissions directly or indirectly, and transports/distributes the substance through e.g. deposition and run-off. This is the case unless, based on the fate and release(s) of the substance, it is considered that the water compartment is not a relevant environmental compartment at all.

In your comments you have supported your reasoning regarding the most relevant compartment with supporting read-across information (addressed above) and Substance properties (i.e. adsorption) reported in your dossier. In particular, you consider that the Substance has high adsorptive potential and uses limited to industrial settings. You refer to an analogue substance with similar uses that is completely removed from sludge and not released to water compartment, and you expect a similar fate for the Substance. However, since you have not demonstrated how the data on the analogue substance is relevant to the Substance (as explained above), you have not demonstrated that there is no exposure to the water compartment for the Substance. In turn, you have not demonstrated that the water compartment is not a relevant compartment for the Substance.

We further remark that the OECD TG 309 (with a default concentration of suspended solids of 15 mg dw/L) minimizes potential NER formation. If NER is formed at significant levels in the OECD TGs 307 and 308 studies, this can be difficult to interpret and compare with degradation half-lives criteria of Annex XIII to the REACH Regulation (ECHA Guidance R.11.4.1.1.1).

Finally, the ECHA Guidance R.11 states that appropriate data needs to be available to conclude on the P/vP-assessment with a conclusion "not P/vP" on all three (five) compartments: water (marine water), sediment (marine sediment) and soil. If a conclusion "P" or "vP" is reached for one compartment, no further testing or assessment of persistence of other environmental compartments is normally necessary (ECHA Guidance R.11.4.1.1.1). In your comments you propose to initiate simulation testing on sediment. As indicated above, you may choose on your own responsibilty to conduct the sediment study first, with appropriate documented justifications based on intrinsic properties, uses, releases, and the compartment considered most likely to provide a worse-case assessment of persistence. Based on the above, the persistency testing can be stopped if a conclusion "P" or "vP" is reached for one compartment for the purpose of PBT/vPvB assessment. However, no conclusion can be made on B and T properties of the Substance as already explained under Appendix A.2-3, B.2 and B.7 of this decision. Therefore, only a conclusion on "vP" can be considered sufficient to stop simulation testing.

You remain responsible for complying with this decision by the set deadline.

Your comments related to tiered testing are further addressed in Appendix E of this decision.

5. Soil 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).

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 (Guidance on IRs and CSA, Section R.11.4.).

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

Further, the Substance has high partition coefficient (log Kow 6.71) and high adsorption coefficient (log $K_{oc,soil}$ of 4.06, indicating high potential to adsorb to soil.

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.

In the comments to the draft decision, you indicate your intention to perform the requested study conditionnally to the results of the OECD TG 308 study requested in Section B.6 of this decision. You indicate that the sediment is the most relevant compartment to test hence you plan to explore ways to address the information requirement for a soil simulation test based on other studies requested in this decision. In particular, you indicate that in the event new data from the study requested in Section B.4 would provide conclusion on P/vP criterion, no further simulation studies would be performed.

Your reasoning regarding the most relevant compartment and when when to stop simulation testing are addressed under Section B.4 above.

As this approach relies on data yet to be generated, ECHA cannot make a conclusion on the need to perform the requested test in order to conclude on P/vP property hence you remain bound to this information requirement.

Your comments related to tiered testing are addressed in Appendix E of this decision.

Study design and test specifications

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.

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).

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.

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.

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.).

6. 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).

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 (Guidance on IRs and CSA, Section R.11.4.).

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

Further, the Substance has high partition coefficient (log Kow 6.71) and high adsorption coefficient (log $K_{oc,soil}$ of 4.06, indicating high potential to adsorb to sediment.

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.

Study design and test specifications

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.

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 (Guidance on IRs and CSA, 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 (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.

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.).

In the comments to the draft decision, you agree to perform the requested study.
Your comments related to tiered testing are addressed in Appendix E of this decision.

7. 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).

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 (Guidance on IRs and CSA, Section R.11.4.).

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

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

In the comments to the draft decision, you agree to perform the requested study as part of the OECD TG 308 requested in Section B.6 of this decision.

Your comments related to tiered testing are addressed in Appendix E of this decision.

Study design and test specifications

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 B.4, B.5 and B.6 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.

8. 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 (Guidance on IRs and CSA, Section R.11.4.).

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

Therefore, the chemical safety assessment (CSA) indicates the need for further investigation on bioaccumulation in aquatic species.

In the comments to the draft decision, you indicate that you "consider the performance of the study as a last resort. Firstly the T and P criteria have to be accordingly assessed and then a bioaccumulation study can be considered. Additionally, the BCF test is an animal test and due to animal welfare, all alternative methods will be considered before an experimental bioaccumulation study is initiated"

Firstly, regarding your intention to conclude on T and P before considering B, ECHA remarks that when information is needed for several PBT properties, the assessment should normally focus on clarifying the potential for persistence first. When it is clear that the P criterion is fulfilled, a stepwise approach should be followed to elucidate whether the B criterion is fulfilled, eventually followed by toxicity testing to clarify the T criterion (ECHA Guidance R.11.4.1).

As already explained above, the information available in your registration dossier indicates the PBT/vPvB potential of the Substance. Clarification of P/vP properties is requested in the present decision (see Sections B 4 to 7). Therefore your proposal to investigate the bioaccumulation of substance only as a very last resort is in line with ECHA Guidance on PBT assessment.

Secondly, regarding your intention to avoid animal testing by adapting this information requirement based on alternative methods, we remark that you have not provided any information relating to a legal basis for adaptation under the REACH Regulation.

As you have not provided any new scientific information that could address the information requirement you remain responsible for complying with this decision by the set deadline.

Your comments related to tiered testing (i.e. conclusion on T prior to P and B) are addressed in Appendix E of this decision.

Study design and test specifications

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.

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 C: 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[7].

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[8].

[7] https://echa.europa.eu/practical-guides
[8] https://echa.europa.eu/manuals

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

A. 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 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 E: Procedure

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 01 February 2021.

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

Deadline to submit the requested information in this decision

In your comments on the draft decision, you requested an extension of the deadline to provide information from 39 to 48 months from the date of adoption of the decision.

Laboratory capacity and analytical difficulties

You have provided a laboratory statements along with your comments in which you based your request for a deadline extension on anticipated delays on concluding all environmental related studies requested in this decision. In particular, analytical difficulties are raised in your comments and supported by the CRO statement. Specifically, it is stated that '*analytical methods and suitable dosing regimen may be difficult to implement in the ecotoxicology studies, and identification of degradation products and quantification of NER might be very challenging in the e-fate studies'*.

ECHA acknowledges that extra time may be needed to develop suitable analytical method(s) and agrees with your request for deadline extension.

Tiered testing strategy

Furthermore, you claim your intention to perform tiered testing and you propose to start by concluding on T before testing P and than B which you consider to be in line with ITS strategy.
As explained in sections B.4 to B.7, your substance screens as potential PBT/vPvB and therefore, the CSA indicates the need for further P and B testing. However, the information on aquatic toxicity requested in sections A.2-3 and B.2 relate only to information requirements at Annexes VII and VIII which do not depend on the PBT assessment. These requests under Annex VII and VIII are not triggered by a concern arising form the PBT assessment. Therefore, studies required for conclusion on T (in particular regarding aquatic toxicity studies) and on P properties are not conditional to one another and can be carried out in parallel.
The deadline set in this decision accounts for all necessary conditional testing hence no additional time is granted for tier testing.
ECHA has extended the deadline to 48 months from the date of 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 F: List of references - ECHA Guidance[9] 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)[10]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[11]

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.

OECD Guidance documents[12]

[9] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[10] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[11] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[12] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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.

Appendix G: 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]
[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.