~~Confidential~~

Helsinki, 02 February 2022

Addressees
Registrants of JS_3457-61-2 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
17/07/2019

Registered substance subject to this decision ("the Substance")
Substance name: tert-butyl α,α-dimethylbenzyl peroxide
EC number: 222-389-8

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 ***7 August 2024***.

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)

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

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

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

3. 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. Extended one-generation reproductive toxicity study (triggered by Annex IX, Section 8.7.3., column 1; test method: OECD TG 443) by oral route, in rats, specified as follows:

   - Ten weeks premating exposure duration for the parental (P0) generation;
   - Dose level setting shall aim to induce systemic toxicity at the highest dose level;
   - Cohort 1A (Reproductive toxicity);
   - Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation

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

3. 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.

4. Identification of degradation products (Annex IX, 9.2.3.; test method: using an appropriate test method)

5. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2; 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 IX 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 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. Triggers for further testing to clarify PBT properties of the Substance

Further testing to clarify degradation and bioaccumulation properties is triggered by the chemical safety assessment (CSA) if the substance is a potential PBT/vPvB substance (Annex VIII, Section 9.2., Column 2 as well as Annex I, Section 4; Annex XIII, Section 2.1). This is the case if the Substance itself or any of its constituents or impurities are present in concentration ≥ 0.1% (w/w) or relevant transformation/degradation product meets the following criteria based on screening information:

- it is potentially persistent or very persistent (P/vP) as:
  - it is not readily biodegradable (i.e. <60% degradation in an OECD 301F), 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).

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

- The Substance is not readily biodegradable (0% degradation after 28 days in OECD TG 301F);
- The Substance has a high potential to partition to lipid storage based on the Log Kow. You provided three Log Kow values for the Substance in the dossier with two exceeding the Log Kow of 4.5, and one being close to the threshold value, indicating high potential to partition to lipid i.e:
  - Log K_{ow} of 4.94 (OECD TG 117; [redacted] 2012)
  - Log K_{ow} of 4.40 ± 0.02 (OECD TG 123; [redacted] 2013)
  - Log K_{ow} of 4.66 (EPI Suite v4.1. QSAR estimate)

In your PBT assessment in Section 2.3 of the registration dossier, you conclude that the Substance is not B/vB since LogKow is <4.5 based on Log Kow of 4.40 (OECD TG 123; [redacted], 2013).

The screening information above indicates that the Substance is a potential PBT/vPvB substance. Furthermore, we have assessed the information provided in your PBT assessment and identified the following issue.

You used only the lowest available Log Kow value (4.40) in your assessment of B/vB potential. But the Log Kow of 4.94 (OECD TG 117; [redacted] 2012, study reliability 1), and the Log Kow of 4.66 (EPI Suite v4.1. QSAR estimate), indicate that the Substance has high potential to partition to lipid.

You state that the HPLC method used to generate the Log Kow of 4.94 (OECD TG 117; [redacted] 2012) overestimates the Log Kow. However, you provide no data to justify that this conclusion is relevant for the Substance.

In the comments to the draft decision, you justify the application of the logKow of 4.40 obtained from the study based on OECD TG 123 (slow-stir method) to be more accurate for the Substance than the logKow of 4.94 derived from a valid OECD 117 (HPLC method), because method on OECD TG 123 would measure directly concentrations of test substance in the water and in octanol, is not dependent on reference substances and because it is performed at room temperature. On the OECD TG 117 study, in turn, you raise concerns in terms of the suitability of the reference substances as well as the temperature used in this study.

Regarding the latter, ECHA notes however that the reference substances used are adequate, listed in the OECD 117 guideline, and covering most of the moieties of the test substance (i.e aromatic ring). Further, OECD 117 guideline does not establish a temperature in which the study should be performed, hence performing the study at 55 °C does not invalide it. Furthermore, literature indicates that logKow does not variate substantially with temperature[2].

To conclude, the arguments raised in your comments do not invalidate the provided OECD TG 117 study results. ECHA notes that both methods are suitable for the Substance and both studies are considered to be valid. Consequently, both studies provide equally reliable and relevant results for the Substance. Therefore, in terms of assessing bioaccumulation properties of the Substance, you did not provide justification as to why you take into account only the lowest of the available logKow values for your assessment.

Hence, available evidence indicates potential for bioaccumulation.

Therefore, your conclusion of the B/vB properties is not reliable and the chemical safety assessment (CSA) indicates the need for further investigation of the PBT/vPvB properties.

The examination of the available information or adaptations, as well as the selection of the requested tests and the tests design are addressed respectively in Appendices C.3-C.5.

[2] https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/pdf/10.1002/sscp.201900033

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. Ames test ([redacted], 1977) with the following strains, TA 98, TA 100, TA 1535, TA 1537, and TA 1538 which all gave negative results.

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[3] (1997). The key parameters of this test guideline includes:

a) 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)

b) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.

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

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

b) a positive control that produced a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control. You indicate that no positive control was used in this test and state that "*the reversion properties of each strain are regularly checked*" using methylmethanesulfonate, 4-aminobiphenyl, 9-aminoacridine, N-mehtyl-N-nitro-N-nitrosoguanidine as positive controls. The OECD TG 471 requires the use of concurrent strain-specific positive and negative controls. Based on the information provided in your dossier, no concurrent positive controls were used in this assay. You referred to historical control data. However, you have not provided any information or results from these historical control data to establish the effective performance of each assay.

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

Therefore, the information requirement is not fulfilled.

In the comments to the draft decision you agree with the request.

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

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

1. 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).

As explained in the Appendix on Reasons common to several requests, the Substance is a potential PBT/vPvB substance and 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 test and the test design are addressed respectively in Appendix C.3.

2. 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 in the Appendix on Reasons common to several requests, 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 further information on the selection of the approach to generate this information are addressed in Appendix C.4.

3. 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).

As explained in the Appendix on Reasons common to several requests, the Substance is a potential PBT/vPvB substance and the chemical safety assessment (CSA) indicates the need for further investigation on bioaccumulation in aquatic species.

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

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

1. Extended one-generation reproductive toxicity study

The basic test design of an extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is a standard information requirement under Annex IX to REACH, if the available repeated dose toxicity studies indicate adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity. Furthermore column 2 defines the conditions under which the study design needs to be expanded.

You have provided a waiving argument whereby you consider that "*In the OECD 422 and OECD 408 studies on tert-butyl cumyl peroxide, no effect on reproductive organ were observed in male and female rats after an oral exposure*".

Your dossier contains the following studies conducted with the Substance:

i. Sub-chronic toxicity study according to the OECD TG 408 ([redacted] 2018), rats, oral route;
ii. Dose range finding study [redacted] 2012), rats, oral route;
iii. Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test according to the OECD TG 422 [redacted], 2013), rats, oral route;
iv. Pre-natal developmental toxicity study according to the OECD TG 414 ([redacted], 2018), rats, oral route.

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

You consider that no adverse effects on reproductive organs or tissues have been observed in the available repeated dose toxicity studies.

However, adverse effects on reproductive organs or tissues or other concerns in relation with reproductive toxicity are observed in available studies. More specifically:

- In study iii: evidence of reduced fertility is reported in the mid and high dose groups. A reduction in the number of oestrous cycle was also observed in females from the high dose group. All these effects were observed in the absence of other significant parental toxicity.
- In study iv: increased incidence of abortions compared to controls was reported. In addition, post-implantation loss was significantly higher in high dose females compared to controls, in the absence of concomitant severe maternal toxicity.

An EOGRT study according to OECD TG 443 as specified in this decision is an information requirement for your registration, because Column 1 criteria at Annex IX, section 8.7.3 are met.

In your comments on the draft decision, you consider that the effects listed by ECHA to trigger the information requirement of Annex IX, 8.7.3 "*do not point at reproductive or developmental toxicity as these were all seen in the presence of marked parental/maternal toxicity, as evidenced by markedly reduced body weight gain and food intake*". In order to support your assessment, you provided tabular data presenting the results obtained on general parameters such as clinical observatins, body weight, food consumption, organ weights obtained from studies i-iv. You also provided detailed information in tabular format on oestrous cycle, implantation, pre-birth loss data and litter data on study iii. and litter data for study iv. In your comments, you also provided details on historical control data on oestrous cycle and fertility index collected from studies conducted on SD rats according to the OECD TGs 421 or 422 over the period 2006-2012.

Based on these comments, ECHA has edited the set of findings triggering the information requirement compared to the initial draft decision, but maintains its above observations on the adverse effects with a view to the following.

Regarding ECHA's findings of adverse effects from study iii, you consider in your comments that the observations on reduced oestrous cycles in females of the high dose group are not statistically significant and remain well within the historical control data for this parameter. Similarly you consider that the fertility index of 80% and 70% noted in the mid-dose and high dose groups, respectively, are within the range of values of the historical control data for this parameter.

According to the OECD Guidance Document 43, paragraph 67, "*Comparison of concurrent study control data with the data from treated animals should always take precedence over comparison with historical control data*". The mean number of oestrous cycles in females of the low and mid dose groups in the study iii. are similar to the mean number of oestrous cycle counted in the concurrent control group. However, the mean number of oestrous cycle counted in females from the high dose group is significantly lower than that of the concurrent control and other test groups. No cycles were observed at all for 1/10 females, 1 cycle and 2 cycles were counted in 2 other animals. Regular oestrous cycle is also an indicator of successful ovulation and variations in oestrous cycles need to be evaluated in conjunction with the reduced fertility index and with the observation of lower mean numbers of coporea lutea and implantations in the high dose group in study iii. However as indicated above, a dose dependent reduction of the fertility index is observed with 80% and 70% noted in the mid-dose and high dose groups whereas in the control and low dose group, the fertility index is 100%.

Historical control data allow detection of abnormal control response, enhance interpretation of study results and inform on background variations observed over time in control animals. To provide reliable and meaningful contribution to the determination of the biological significance of effects observed in a study, the OECD Guidance Document 43 requires that the historical control data are collected "*within a reasonable amount of time prior to the study being interpreted (e.g., ± 2 years) in order to avoid genetic drift in the laboratory animal population*". The study iii. was conducted in 2012. The historical control data that you provided in your comments have been collected over a 6-year period, i.e. between 2006-2012, and report wide minimum and maximum ranges and values. This affects the reliability of the conclusions which can be derived from these historical control data for both of the number of oestrous cycle and fertility index. Therefore, as indicated in the OECD Guidance Document 43, the concurrent study control data do take precedence over the historical control data in order to derive reliable conclusions on the biological significance of the effects observed in the high dose group in study iii.

In your comments to the draft decision you consider that the findings related to reproductive and developmental toxicity are "*observed at these high doses do not point at reproductive or developmental toxicity as these were all seen in the presence of marked parental/maternal toxicity*". In addition, for study iii. you specify that the effects noted by ECHA are not statistically significant and all secondary to the dams' "*marked impaired health condition in view of their markedly reduced BW gain and food intake*".

The terminal body weight of high dose females was measured to be 18% lower than that of the control animals. No reduction in body weight gain or food consumption was detected during the pre-mating period and up until gestation day 7 for females of the high dose group in study iii. Based on the information provided in your technical dossier and in your comments, the reduction in body weight gain and in food consumption was reported starting from

gestation day 7 and gestation day 14, respectively, and continued until the end of the exposure period in study iii.

While a reduction in body weight constitutes evidence of toxicity, its time of onset and extent does not indicate severe maternal toxicity likely to have affected the oestrous cyclicity and the successful ovulation. Indeed, as monitoring of the oestous cycles occurred during the pre-mating period and up until evidence of mating and the ovulation occurs at the time of the mating, no correlation can be established between the reduction in oestrous cycle, the reduction in the number of corporea lutea in the dams of the high dose group and maternal toxicity. Similarly no direct correlation between the occurrence of these findings and the hepatotoxicity and thymus toxicity detected at the end of the study in high dose females can be established.

Furthermore, the increased incidence of abortions and post-implantation losses observed in the high dose group of study iv. were only detected in the presence of moderate maternal toxicity evidenced in the form of reduced terminal body weight of 12% in comparison to control.

The OECD Guidance Document 43 states that "*statistical significance does not need to be present to validate the biological significance of treatment-related effects*". In this specific case, ECHA considers that the reduction in oestrous cycles, the reduced fertility index, and the lower mean numbers of copora lutea leading to lower number of implantations and to a lower litter size detected in the high dose group of study iii. and the post-implantation losses and increased incidence of early resorptions detected in the high dose group in study iv. cannot be considered as secondary to maternal toxicity based on the information provided in your dossier and in your comments. Therefore, even though some of these effects did not reach statistical significance ECHA considers that these findings constitute a consistent body of evidence indicating a concern in relation to reproductive toxicity.

Based on the above, your waiving argument is not acceptable and the information you provided does not fulfil the information requirement.

<u>The specifications for the study design</u>

Premating exposure duration and dose-level setting

The length of premating exposure period must be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required to obtain results adequate for classification and labelling and /or risk assessment. There is no substance specific information in the dossier supporting shorter premating exposure duration[4].

Therefore, the requested premating exposure duration is ten weeks.

In order to be compliant and not to be rejected due to too low dose levels, the highest dose level shall aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects. A descending sequence of dose levels should be selected in order to demonstrate any dose-related effect and to establish NOAELs.
If there is no relevant data to be used for dose level setting, it is recommended that range-finding results are reported with the main study.

[4] ECHA Guidance R.7a, Section R.7.6.

You have to provide a justification with your study results that demonstrates that the dose level selection meets the conditions described above.

Cohorts 1A and 1B

Cohorts 1A and 1B belong to the basic study design and must be included.

Cohorts 2A and 2B

ECHA agrees that the conditions to the include the Cohorts 2A and 2B in the design of this study are currently not met.

Species and route selection

The study must be performed in rats with oral[5] administration.

Further expansion of the study design
The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohort 2A and 2B and/or Cohort 3 if relevant information becomes available from other studies or during the conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Column 2, Section 8.7.3., Annex IX. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in ECHA Guidance[6].

2. 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 the following information:

- 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 provided the following justification:

> *'A long-term toxicity testing on aquatic invertebrates has been performed ([redacted] 2018) following the final decision of ECHA on testing proposals (ECHA decision number TPE-D-2114319122-65-01/F). Indeed, based on acute aquatic toxicity data, neither fish nor daphnia are shown to be substantially more sensitive. Therefore, according to the integrated testing strategy, the long-term daphnia study has been conducted first. Based on the results of this test and the application of the relevant assessment factor, no risks are observed (PEC/PNEC<1) for the aquatic compartment. Therefore, in accordance with the ECHA guidance (Chapter R7b, version 2.0 Figure R.7.8-4) and the final decision of ECHA, no long-term fish testing need to be conducted.'*

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

[5] ECHA Guidance R.7a, Section R.7.6.2.3.2.
[6] ECHA Guidance R.7a, Section R.7.6.

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.

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

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.).

The Substance may be difficult to test due to the low water solubility (10.66 mg/L) and adsorptive properties (based on: Log Kow 4.40-4.94). OECD TG 210 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 210. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

3. 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 Annex IX, Section 9.2., Column 2 with the following justification:

'*The substance does not fulfil the PBT or vPvB criteria as the log Kow value of the substance has been determined to be 4.4 (OECD 123). [..] In addition, the PEC/PNEC ratio for the aquatic compartment obtained in the exposure assessment of the substance is below 1. [..]*'

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). This is the case if the Substance itself or any of its constituent, impurity or transformation/degradation product present in concentration ≥ 0.1% (w/w) meets the criteria already listed in the Appendix on Reasons common to several requests.

As already explained in the Appendix on Reasons common to several requests, the Substance is a potential PBT/vPvB substance. Therefore, you have not demonstrated that the CSA does not indicate the need for further biotic degradation testing and your adaption is rejected.

In the comments to the draft decision, you agree that there is a need to further biotic degradation testing. However, you raise concerns in regards to technical feasibility of the requested study due to the Substance properties, i.e. its volatility. There is currently no explicit adaptation or Substance specific evidence available in the dossier, or provided in your

comments to the draft decision, to demonstrate that omission of the study was justified in accordance with Annex XI Section 2, Testing is technically not possible. In paragraph 7 of OECD TG 309 it is specified that the test is applicable for non-volatile or slightly volatile substances (Henry´s law constant < 100 Pa m3/mol), however, the use of closed flasks with a headspace should be considered in order to prevent losses from the test system.

In your comments, you propose a tiered testing approach in which you intend to first investigate whether a study according to OECD TG 309 is technically feasible and, if this was not the case, conduct an OECD TG 308 study instead. Your considerations are based on data yet to be generated and ECHA is not in the position to assess this information and no conclusion on the compliance can currently be made. You remain responsible for complying with this information requirement by the set deadline (by providing the standard information or a valid adaptation). As far as you may suggest possible other investigations, you are reminded that before conducting a study listed in Annex IX or Annex X, and not yet requested by this decision, such as a study according to OECD TG 308, a testing proposal must be submitted.

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.).

4. Identification of degradation products

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

You have provided no information on the identity of transformation/degradation products for the Substance.

Therefore, this information requirement is not met.

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

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 Kow and potential toxicity of the transformation/degradation may need to be investigated. You may obtain this information from the degradation study requested in Appendix C.3 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.3) 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).

5. Bioaccumulation in aquatic species

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

You have provided the following information:

i. an adaptation according to Annex XI, Section 1.3, by providing results from a (Q)SAR prediction: BCFBAF model v3.01 from EPI Suite v4.1.

We have assessed this information and identified the following issues:

Annex XI, Section 1.3. specifies that 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(s):

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

With regard to point '4' above, 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:

- model prediction, including the endpoint,
- relationship between the modelled substance and the defined applicability domain,
- close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

You have not provided documentation for the prediction, in the form of QPRF.

In the absence of adequate and reliable documentation of the method, it cannot be confirmed that

- the Substance is within the applicability domain of the model;
- the prediction is reliable, since no information provided on model prediction (including justification for the selection of the submodel used within the BCFBAF model v3.01) nor on close analogues.

In absence of such information, ECHA cannot establish that all the conditions of Annex XI, Section 1.3. are met and the prediction can be used to meet this information requirement.

B. *The prediction is not adequate due to low reliability*

With regard to point '3' above, 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 cumulative conditions must be met (among others):

- reliable input parameters are used, and
- the prediction is consistent with information available for other related endpoint(s).

Your registration dossier provides the following information:

- a BCF estimate of 372 kg/L (BCFBAF model v3.01, Meylan Model, from EPI Suite v4.1) based on the Log Kow 4.40 (OECD TG 117; [redacted], 2013).

The following information is also available for the Substance used as input for the prediction:

- Log Kow of 4.94 (OECD TG 117; [redacted] 2012),
- Log Kow of 4.66 (EPI Suite v4.1. QSAR estimate).

The prediction for the Substance is not reliable because you have used only the lowest Log Kow available as input to the model. You have not used the experimental Log Kow of 4.94 (study reliability of 1) in your assessment which would provide a worst-case assessment for BCF.

Therefore, you have not demonstrated that the prediction you provided for the Substance is adequate for the purpose of classification and labelling and/or risk assessment.

In the comments to the draft decision, you provide justification as to why you believe that the logKow of 4.40 is considered more accurate for the Substance than logKow of 4.94. But, as explained above in the Appendix on Reasons common to several requests, none of your points raised invalidate the provided OECD 117 study providing a logKow of 4.94.
Therefore, in terms of input parameter, you did not apply reasonable worst case assumptions.

In any case, the lack of a B/vB classification does not fulfil any of the conditions set in the provisions to adapt this information requirement.
In your comments to the draft decision, you further refer to bioaccumulation properties of an analogue substance *a mixture of 1,3-bis(tert-butylperoxy isopropyl)benzene and 1,4-bis(tert-butylperoxy isopropyl)benzene (CAS 25155-25-3)*. ECHA notes that you did not provide any further information to justify the use of a read-across approach in accordance with Annex XI, Section 1.5.

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[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 E: 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 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 01 February 2021.

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

ECHA took into account your comments and did not amend the request(s).

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[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 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]
[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.