Helsinki, 07 January 2022

Addressees
Registrant(s) of Phenol, isopropylated, phosphate (3:1) listed in the last Appendix of this decision

Registered substance subject to this decision (the Substance)
Substance name: Phenol, isopropylated, phosphate (3:1)
EC number: 273-066-3
CAS number: 68937-41-7

Decision number: Please refer to the REACH-IT message which delivered this communication (in format SEV-D-XXXXXXXXXX-XX-XX/F)

DECISION ON SUBSTANCE EVALUATION

Under Article 46 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below:

A. Information required to clarify the potential risk related to PBT/vPvB

1. Ready biodegradability - test methods suitable for poorly soluble substances: CO_2 evolution test (OECD TG 301B), **or** modified MITI(I) test (OECD TG 301C), **or** manometric respirometry test (OECD TG 301F), **or** CO_2 in sealed vessels (headspace test; OECD TG 310), with eleven selected constituents of the Substance, specified as follows:
    - the eleven selected constituents must be tested separately;
    - the tests must be modified to improve the bioavailability of the constituents;
    - the tests may be enhanced by increasing test vessel size;
    - the duration of the test must not be extended beyond 28 days;
    - the following eleven constituents must be tested:

Constituent	EC/ List no	CAS RN
Mono-isopropylated triphenyl phosphate constituents		
phosphoric acid, 2-(1-methylethyl)phenyl diphenyl ester	-	64532-94-1
phosphoric acid, 3-(1-methylethyl)phenyl diphenyl ester	-	69515-46-4
phosphoric acid, 4-(1-methylethyl)phenyl diphenyl ester	-	55864-04-5
Di-isopropylated triphenyl phosphate constituents		
phosphoric acid, bis[2-(1-methylethyl)phenyl] phenyl ester	-	69500-29-4
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
Tri-isopropylated triphenyl phosphate constituents		
[redacted]	[redacted]	[redacted]
tris(3-isopropylphenyl) phosphate	276-759-9	72668-27-0
[redacted]	[redacted]	[redacted]

Deadline

The information must be submitted by

- either **12 October 2022**
- or **14 April 2023 if you can** sufficiently demonstrate, providing supporting documentary evidence of an exhaustive search and of correspondence with the test material providers, that not all specified test constituents are commercially available and must be first synthesized.

Conditions to comply with the information requested

To comply with this decision, you must submit the information in an updated registration dossier by the deadline indicated above. The information must comply with the IUCLID robust study summary format. You must also attach the full study report for the corresponding studies in the corresponding endpoint of IUCLID.

You must update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

You will find the justifications for the requests in this decision in the Appendix entitled ''Reasons to request information to clarify the potential risk'.
You will find the procedural steps followed to reach the adopted decision and some technical guidance detailed in further Appendices.

Appeal

This decision 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.

Basis for substance evaluation

The objective of substance evaluation under REACH is to allow for the generation of further information on substances suspected of posing a risk to human health or the environment ('potential risk').

ECHA has concluded that further information on the Substance is necessary to enable the evaluating Member State Competent Authority (MSCA) to clarify a potential risk and whether regulatory risk management is required to ensure the safe use of the Substance.

The ECHA decision requesting further information is based on the following:

(1) There is a potential risk to human health or the environment, based on a combination of hazard and exposure information;
(2) Information is necessary to clarify the potential risk identified; and
(3) There is a realistic possibility that the information requested would allow improved risk management measures to be taken.

The Appendix entitled 'Reasons to request information' describes why the requested information is necessary and appropriate.

Appendix A – Reasons to request information to clarify the potential risk related to PBT/vPvB properties

0. Overall assessment / testing approach

According to ECHA Guidance R.11.4.1, a constituent is normally to be considered relevant for the PBT/vPvB assessment when present in a concentration of ≥0.1% (w/w). The Substance is a UVCB containing a wide variety of phosphate esters that have been derived from phenol and isopropylated phenol. The constituents differ in their level of isopropylation, ranging from full isopropylation where on each of the three phenols three isopropyl groups are located, to the non-isopropylated triphenyl phosphate (TPP - EC no 204-112-2, CAS RN 115-86-6). Neither the concentrations of individual constituents nor the concentrations of isopropylated TPP constituent groups have been specified, except for the sum of tri-, tetra, and penta-isopropyl phenyl groups.

ECHA notes that the available information does not allow to conclude with certainty which constituents or constituent groups are present at ≥0.1% w/w. However, as several mono--, di-, tri-, and tetra-isopropylated TPP compounds are specified on the ECHA dissemination website as constituents of the Substance, the respective constituent groups are considered present at concentrations of ≥0.1 % w/w. ECHA considers that the mono-, di-, tri- and tetra-isopropylated constituent groups are relevant for the purpose of the PBT/vPvB assessment.

For each level of isopropylation, the individual compounds differ in the position of the isopropyl group(s) on the phenol ring, but also with respect to the distribution of the isopropyl groups over the phenol rings. While there is considerable structural similarity between the compounds within each level of isopropylation, these differences can still affect the PBT/vPvB properties of the individual compounds.

Experimental biodegradation data was only available for two constituents of the Substance. TPP was shown to be readily biodegradable, while a tri-isopropylated TPP constituent showed no degradation in a ready biodegradation test. For this reason, there is no PBT/vPvB concern for TPP, whereas the study with the tri-isopropylated TPP constituent was not sufficient to reach a conclusion on the persistence of the respective constituent.

Using QSAR models it was not possible to determine with certainty the worst-case constituent(s) of the Substance. None of the constituents are predicted to be readily biodegradable. Experimental bioaccumulation data are available for the Substance, the constituent TPP and the mono-isopropylated TPP constituent group. TPP was shown not to bioaccumulate to a large extent, while for the mono-isopropylated TPP constituent group the reported BCF values exceed the B criterion. QSARs predict that the di- and tri-isopropylated TPP constituent groups of the Substance have the highest potential for PBT/vPvB properties based on their higher bioaccumulation potential.

The bioaccumulation potential of the mono-isopropylated TPP constituent group was predicted to be lower due to expected metabolism but could not be excluded, as the estimated log K_{ow} values exceed the screening criterion of 4.5. Furthermore, experimental data suggest a bioaccumulation potential.

Bioaccumulation of the constituent group with four isopropyl groups could also not be excluded as the log K_{ow} values range 8.56-10.52 depending on the applied QSAR model. The constituent groups with five or more isopropyl groups were consistently predicted to

have log K_{ow} >10. The latter constituent groups are therefore considered to have a rather low bioaccumulation potential due to their physical and chemical properties (i.e., high molecular weights and large cross-sectional diameters of some components), low uptake potential and hence low predicted BCF values.

Considering the above, the P assessment of the Substance is targeted to those mono-, di- and tri-isopropylated TPP constituent groups of the Substance, which are expected to have the highest bioaccumulation potential.

The requested data will enable to conclude whether the mono-, di- and tri-isopropylated TPP constituent groups are not to be considered P/vP. If this cannot be concluded, the requested data are expected to indicate the worst-case constituents to be selected for further testing.

1. Potential risk

1.1 Potential hazard of the Substance

Following its assessment of the available relevant information on the Substance, the evaluating MSCA and ECHA have identified the following potential hazard(s) which must be clarified.

a) [Potential] P/vP properties

If a substance fulfils the criteria in Section 1.1.1 or 1.2.1 of Annex XIII to REACH, it is considered that it has persistent (P) or very persistent (vP) properties.

For the purpose of the P/vP assessment and to check whether the criteria are fulfilled, the information listed in Section 3.2.1 to Annex XIII, including results from simulation tests, must be considered.

If no such data are available, it is necessary to consider the screening information of Section 3.1.1 to Annex XIII, such as screening tests and QSAR predictions.

The available information suggest that the Substance may have P/vP properties.

Evidence based on experimental data

No degradation simulation tests referred to in Annex XIII, Section 3.2.1(a), (b) or (c) are available for the Substance.

In the registration dossier of the Substance degradation data are available for several commercial products that correspond to the Substance. Additionally, the UK environmental risk evaluation report (UK-RER) on isopropylated triphenyl phosphate (Brooke et al., 2009) reports data for several other associated commercial products. The Reofos products, i.e. Reofos 35, 50, 65, 95 and 120, contain TPP and (non-specified) isopropylated triphenyl phosphates. Their TPP content is 35, 28-32, 20, 9, and 7.5%, respectively. While the ratio of TPP to isopropylated triphenyl phosphates differs, the Reofos products have the same CAS number as the Substance in their respective data sheets (Lanxess, 2021a; b; c; d).

Other commercial products include [redacted] & 1000, Phosflex 31P and Durad 300 & 310M. For the [redacted] products more details on the composition are provided in the UK-RER specifying the mono-, di- and tri-isopropylated TPP constituent groups. Their TPP content ranges from 4 to 33%. The Durad products have 4-5% TPP, and Phosflex 31P 28-30% TPP, and their isopropylated triphenyl phosphates are not specified.

Hydrolysis data

- The registration dossier of the Substance contains a hydrolysis study for the commercial product Reofos 65 conducted according to OECD TG 111 where hydrolysis was measured as a function of pH. Reofos 65 is hydrolytically stable at pH 4, but increasingly unstable with increasing pH. The hydrolysis half-life at ambient temperature and pH was considered 18.5 days (25°C; pH 7). Analytical monitoring was performed with GC/MS, but from the robust study summary it could not be determined what was actually measured. As indicated above Reofos 65 consists of 20% of TPP while the remaining 80% consists of non-further specified isopropylated triphenyl phosphates. It remains unclear to what extent the hydrolysis can differ depending on the isopropylation. ECHA further notes that the hydrolysis was also determined at 15°C, which approximates the European average temperature of 12°C, and the half-live values amounted to 42.6 days at pH 7 and 16.5 days at pH 9. Normalisation to 12°C yields for pH 7 hydrolysis half-live values of 57 and 62 days and at pH 9 20 and 22 days based on the tests conducted at 25 and 15°C, respectively.

- The registration dossier of TPP contains a hydrolysis study where hydrolysis was measured as a function of pH for commercial products, but also TPP alone. Analytical monitoring was included. Based on the test with TPP alone, hydrolysis half-live values of >28, 19 and 3 days were obtained at 25°C and pH 5, 7 and 9, respectively. Normalisation to 12°C yields hydrolysis half-live values of >93, 63 and 10 days, respectively.

Considering both hydrolysis studies it can be concluded that the constituent TPP as well as the commercial product Reofos 65 do not hydrolyse rapidly under realistic European environmental conditions with the hydrolysis half-live values being above 40 days at 12°C at pH 7. Furthermore, no conclusions can be drawn from the study conducted with Reofos 65 regarding the hydrolytic stability of the individual isopropylated constituents, nor how the level of isopropylation affects hydrolysis. Finally, hydrolysis studies alone are not deemed sufficient to exclude persistence of a substance under environmentally realistic conditions.

Ready biodegradability data

- The registration dossier of the Substance contains a closed bottle test according to OECD TG 301D for the commercial product Reofos 65. After 28 days, biodegradation amounted to 18% based on theoretical oxygen demand (ThOD) showing that Reofos 65 is not readily biodegradable. The study was conducted at 2.1 mg/L, whereby the test substance was directly added to the test vessels followed by sonification for 5 minutes to ensure a good dispersion. It is not reported if the test vessels were stirred and/or agitated during testing, which is recommended in the test guideline for poorly soluble substances. Reofos 65 has a water solubility of 0.33 mg/L at 20°C in HPLC-grade reagent water as determined by the flask methodology according to OECD TG 105. Using the same methodology, a water solubility of 0.367 mg/L has been determined for the commercial product Reofos 35 (TPP content of 35%). Both studies reported that analytical monitoring was conducted with GC/MS but no details were provided and it is unclear what was actually measured. It can be expected that the more isopropylated constituents with increasingly higher log K_{ow} values will have correspondingly lower water solubilities. The bioavailability of the more isopropylated constituents may thus have been limited in this study.

- The registration dossier of the constituent TPP contains a modified MITI(I) test according to OECD TG 301C for TPP, showing that TPP is readily biodegradable with

biodegradation amounting to 83-94% within 28 days based on the biochemical oxygen demand (BOD). The study was conducted at a default test concentration of 100 mg/L. The water solubility of TPP was experimentally determined to be 1.9 mg/L. The exceedance of the water solubility in the test is not considered a major issue as TPP is bioavailable at the start, and any biodegradation will result in solubilisation of the undissolved fraction making it bioavailable during the test. ECHA considers TPP readily biodegradable.

- In the J-CHECK database, a modified MITI(I) test according to OECD TG 301C is available for the tri-isopropylated TPP constituent, tris[4-(1-methylethyl)phenyl] phosphate (NITE, 1984a). Biodegradation amounted to 0% within 28 days based on BOD and parent substance analysis by HPLC/UV-VIS. The study was conducted at a default test concentration of 100 mg/L. The exceedance of the water solubility is very high with a predicted water solubility for the tri-isopropylated TPP constituent of 0.026 µg/L (WSKOW). The study report does not specify if the test material was dispersed (e.g. using very finely ground material or ultrasonics). Therefore, while the test shows that the tri-isopropylated TPP constituent is not readily biodegradable, this could at least partially be due to a very low bioavailability.

- The UK-RER on isopropylated triphenyl phosphate reports several additional ready biodegradation studies conducted with commercial products associated with the Substance. These studies were obtained in 2000 from IUCLID, but are not present in the registration dossier of the Substance.
  - For Reofos [redacted], a modified Sturm test according to OECD TG 301B is available where mineralization amounted to 74 and 80% after 28 days at 10 and 20 mg/L, respectively. Reofos 50 is considered readily biodegradable. Reofos [redacted] is indicated by the same CAS number as the Substance in in its data sheet ([redacted], 2021b).
  - For Reolube [redacted], three ready biodegradation tests were available: a DOC die-away test according to OECD TG 301A showing 86% mineralization after 31 days at a test concentration of 32.6 mg/L; a modified Sturm test according to OECD TG 301B showing 29 and 40% mineralization after 28 days at test concentrations of 10 and 20 mg/L; and a manometric respirometry test according to OECD TG 301F showing 46% mineralization after 28 days (test concentration not reported). The results of the DOC die-away test should be treated with caution as the test is not intended for the testing of poorly water soluble substances. Based on the results of the other studies, Reolube [redacted] is considered not readily biodegradable. While Reolube is specified as a trade name of the Substance in the registration dossier of the Substance, it remains unclear to what extent Reolube [redacted] corresponds to Reolube.
  - For Reofos [redacted], two ready biodegradation tests were available: a modified Sturm test according to OECD TG 301B showing 21 and 13% mineralization after 28 days at test concentrations of 11 and 22 mg/L; and a manometric respirometry test according to OECD TG 301F showing 47% mineralization after 28 days. Extending the test to 68 days resulted in >60% mineralization. In the UK-RER, the prolonged test was considered to point towards inherent biodegradability. Reofos [redacted] is considered not readily biodegradable.
  - For [redacted], a non-guideline river die-away test is available that reported 80% primary degradation after 28 days based on GC analysis of the sum of the major components present in the test substance. No significant degradation was seen in the sterile controls. This test suggests that the Substance at least undergoes primary degradation. The study investigated biodegradation using two additional methodologies that are not suitable for the P assessment and that are not further discussed, i.e. primary degradation using

a semi-continuous activated sludge unit and ultimate mineralization using adapted inoculum according to a modified Sturm method.

Considering above, it can be concluded that the constituent TPP is readily biodegradable (83-94% biodegradation after 28 days in OECD TG 301C) and that there is no P concern for TPP.
The tri-isopropylated TPP constituent tris[4-(1-methylethyl)phenyl] phosphate showed no biodegradation in a modified MITI(I) test within 28 days, which could be in part due to very low bioavailability.
For the Substance no unequivocal results were obtained, i.e. ready biodegradability was reported for Reofos [redacted] (74-80% biodegradation after 28 days in OECD TG 301B), while no ready biodegradability was reported for Reofos [redacted] (18% mineralization after 28 days in OECD TG 301D) and Reofos [redacted] (13-21% mineralization after 28 days OECD TG 301B; 47% after 28 days and >60% after 68 days in OECD TG 301F). The results obtained with the Reofos products show that products with a higher content of isopropylated TPP constituents are less biodegradable. The variation in degradation observed with the different commercial products could be related to differences in composition, differences in inoculum, but also to bioavailability issues of the isopropylated TPP constituents. Overall, these studies do not allow to conclude on the biodegradability of individual isopropylated TPP constituents.

Literature data

- The UK-RER on isopropylated triphenyl phosphate reports a non-guideline 28-day water/sediment simulation study from public literature for the mono-isopropylated TPP constituent isopropylphenyl diphenyl phosphate (IPDP) (Heitkamp et al., 1984). The study was conducted with di[^{14}C]phenyl- and isopropyl[^{14}C]phenyl ring-labelled IPDP at 15.6 and 585 µg/L. The test was conducted under aerobic and anaerobic conditions at 22±1 °C. Treatments were conducted in quintuplicate in 250-mL glass flasks each containing 10 g moist lake sediment and 90 mL of accompanying water (pH 7.1) to which test substance dissolved in 50 µL acetone was added. A sterile control was included to detect abiotic degradation. Evolved $^{14}CO_2$ was trapped and weekly quantified by liquid scintillation counting (LSC). Volatilization was monitored, but volatiles were not detected. At test end, the supernatants and sediments were extracted with methylene chloride, quantified by LSC and analysed by GC with a flame photometric (FPD) or a thermionic specific detector (TSD). The high dose sediment was also re-extracted with methanol and further analysed by GC-FPD and GC-MS after separation by preparative HPLC. The mass balances ranged 82 to 96% applied radioactivity (AR), the total $^{14}CO_2$ production at test end averaged 7.1-8.4% AR in the di[^{14}C]phenyl-labelled IPDP treatments, 1.1-2.0 in the isopropyl[^{14}C]phenyl labelled IPDP treatments, and there was no $^{14}CO_2$ production in the sterile control. At test end the total of extracted residues in water and sediment averaged 76-87% AR and the total non-extractable residues in sediment averaged 2.7-9.2% AR over the treatments. The study showed that the diphenyl moiety of IPDP mineralized faster than the isopropylphenyl moiety. The oxygen tension and the test concentration hardly affected IPDP mineralization. At test end, the majority of IPDP remained undegraded with relatively non-polar metabolites representing only a small amount of the applied radioactivity. The additional analysis of the high dose sediment showed that polar metabolites (incl. diphenyl phosphate) accounted for around 2.4 to 3.9% AR, and the non-polar metabolite TPP to 3.4-13% AR. DT50 values were not reported.
  ECHA could not calculate DT50 values for the isopropyl[^{14}C]phenyl labelled IPDP treatments due to the low level of mineralization reported. For the di[^{14}C]phenyl-labelled IPDP treatments DT50 values of 212-257 days could be extrapolated using first order kinetics and $^{14}CO_2$ production over time (parent substance was only

quantified at test end). Normalizing these values to 12°C yields DT50 values of 450-546 days, respectively. It should be noted that this study did not report all relevant details, e.g. organic carbon content of the sediment, the viability of the sediment (microbial biomass at test start and end), water quality parameters, etc. Furthermore, the DT50 values have been extrapolated far beyond the duration of the test and are based on CO_2 production, excluding any primary degradation. Therefore, these data are considered only as indicative for the persistence of IPDP, i.e. the mono-isopropylated TPP constituent group of the Substance.

Evidence based on model predictions

BIOWIN models were used to predict whether the screening criteria for P and vP (ECHA Guidance R11) are fulfilled for the mono-, di-, tri-, and tetra-isopropylated constituents of the Substance. The molecular weight of these constituents ranges from 368.4 to 494.6 g/mol, which is within the applicability domain of all BIOWIN models (narrowest range is 53.06 to 697.7). All models contain 'phosphate ester' and 'unsubstituted phenyl group' as molecular fragment in their training set, supplemented with '-CH_2-' and '-CH_3' in models 5-7. All BIOWIN models are considered relevant.
The mono-, di-, tri-, and tetra-isopropylated constituents were predicted to be not readily biodegradable, indicating that the Substance may have P/vP properties.

Conclusion on the available information

The available information is not sufficient to draw a conclusion on the potential hazard. Further information is needed on the P/vP properties of the mono-, di- and tri-isopropyl substituted constituents of the Substance.

b) [Potential] B/vB properties

If a substance fulfils the criteria in Section 1.1.2 or 1.2.2 of Annex XIII to REACH, it is considered to have bioaccumulative (B) or very bioaccumulative (vB) properties. For the purpose of the B/vB assessment and to check whether the criteria are fulfilled, the information listed in Section 3.2.2 of Annex XIII must be considered, including bioconcentration factor (BCF) values. Notably, if the BCF value is > 2000 or > 5000, the Substance fulfils the criteria for B or vB, respectively. If no such data is available, it is necessary to consider the screening information of Section 3.1.2 to Annex XIII.

Section 3.1.2 of Annex XIII specifies that the indicator for the screening of bioaccumulation potential is the Log K_{ow} determined experimentally or estimated by (Q)SAR models, provided the models fulfil the criteria of Annex XI, Section 1.3. The threshold value for bioaccumulation potential provided in Section R.11.4.1.2.10 of REACH Guidance R.11 is a Log K_{ow} value higher than 4.5.

Because the focus of the decision is on the P/vP properties, the existing information on the bioaccumulation potential of the substance is only shortly summarised following the evaluating MSCA's assessment.

Evidence based on experimental data

- The registration dossier of the Substance reports for TPP a log K_{ow} of 4.92 and log K_{ow} values of 4.93, 5.18 and 5.08 for the commercial products [redacted]. ECHA notes that the log K_{ow} of 4.92 reported for TPP is higher than the log K_{ow} of 4.63 determined in the shake-flask study with TPP (key study in the TPP registration dossier). Regarding the commercial products, it is unclear on which constituents these log K_{ow} values are based and how the measurements were conducted. Overall, the reported log K_{ow} values are not considered reliable.

- The registration dossier of the Substance contains a flow-through fish bioaccumulation test with bluegill according to OECD TG 305 for the commercial product Reofos 35. Mean measured test concentrations were 3.1 and 24 µg/L. Growth-corrected and lipid-normalized whole fish steady state BCF values of 512 and 634 L/kg, and kinetic BCF values of 516 and 559 L/kg are reported for the low and high treatments, respectively. Although not reported, it is assumed that the tested substance consisted for 35% of TPP and 65% isopropylated TPP constituents. The extent of isopropylation of the different constituents is unknown. As the analysis was based on the sum of constituents, this study does not provide information on the bioaccumulation potential of the individual constituents. It is considered unlikely that the different constituents will have the same bioconcentration potential due to increasing log K_{ow} with increasing level of isopropylation and therefore this study is not suited to draw a conclusion whether the B criteria are met or not.

- The registration dossier of the constituent TPP contains several non-guideline studies that reported BCF values ranging 110-18900 L/kg. The key bioaccumulation study reported for TPP a BCF of 144 L/kg in killifish and a rapid elimination upon depuration (<limit of detection within 24 hours).

- A Japanese MITI BCF study is available for the tri-isopropylated constituent tris[4-(1-methylethyl)phenyl] phosphate (NITE, 1984b). The study was performed with carp under flow through conditions for 6 weeks at mean measured exposure concentrations of 0.2 and 2 mg/L. A dispersant was used at 6 and 60 mg/L, respectively. The study reported a BCF of 33 L/kg wwt for the low treatment. ECHA notes that the test concentrations greatly exceeded the predicted water solubility of 0.026 µg/L (WSKOW). Possibly dispersed substance was measured instead of dissolved substance. Based on the predicted water solubility the BCF values should have been much higher. For this reason, ECHA considers the study not reliable.

- The UK-RER on isopropylated triphenyl phosphate reports a 90-day partial life-cycle toxicity study from 1986 conducted under flow-through conditions with fathead minnows and the commercial products [redacted] and Phosflex 31P. Mean measured exposure concentrations (sum TPP and mono-isopropylated TPP) ranged 0.005 to 0.088 mg/L for [redacted], and 0.008 to 0.205 mg/L for Phosflex 31P. The BCF values determined at concentrations ≤NOEC ranged from 861-1667 L/kg for TPP and 6133-9250 L/kg for mono-isopropylated TPP in the test with [redacted], and 800-4000 L/kg for TPP and 6167-8250 L/kg for mono-isopropylated TPP in the test with Phosflex 31P. In the depuration phase, both components had half-lives of <7 days in fish. ECHA notes that while tests were conducted with UVCB substances, BCF values are based on measured concentrations of the individual constituents, and as such the BCF values are suitable for the PBT/vPvB assessment. However, the study was not conducted according to OECD TG 305 and the control survival was relatively poor in the tests with [redacted]. At higher test concentrations, treatment-related toxic effects were reported, but these concentrations have not been used to calculate BCF values. While at most concentrations BCF values for TPP are below the B criterion, values as high as 4000 L/kg are reported. Overall, the BCF values reported in this study provide strong evidence that one or more constituents of the mono-isopropylated TPP constituent group of the Substance are very bioaccumulative (vB).

Evidence based on model prediction

- The registration dossier of the Substance reports QSAR predictions for bioconcentration factors (BCFs) generated by VEGA as supporting evidence based on the CAESAR model and the BCFBAF regression-based model. The calculations are based on 50 constituents that were randomly selected from the 4096 potential structures of the UVCB, and ranged 9-140 and 3.2-998 L/kg wwt, for the two models respectively. The CAESAR model uses three approaches of which you considered the chemical descriptor approach that predicted a BCF of 13.7 L/kg, as not reliable. You reported that "*similar molecules found in the training set have experimental values that strongly disagree with the target compound predicted value*". ECHA notes that the training set of the CAESAR model does not contain substances that are having a close structural resemblance to the constituents of the registered substance. For the test set the BCF value of the tri-isopropylated constituent tris[4-(1-methylethyl)phenyl] phosphate was used, which is considered unreliable as discussed above. Therefore, in this case the CAESAR model is not suited to make a reliable prediction of the bioaccumulation potential of the constituents of the Substance.

- The BCF value could be predicted based on the log K_{ow}. When using KOWWIN log K_{ow} values of 6.16, 7.61 and 9.03 are predicted for the mono-, di-, and tri-isopropylated constituents, respectively. KOWWIN predictions do not differ between isomers of the same constituent group, regardless of the position of isopropyl groups on the phenol ring, or the distribution of isopropyl groups over the phenol rings. In contrast, the ClogP model (BioLoom) does take the position and distribution of the isopropyl groups into account, and predicts log K_{ow} values of 5.48-5.88, 6.51-6.91, 7.54-8.74, and 8.56-9.36 for the mono-, di-, tri-, and tetra-isopropylated TPP constituents, respectively. The predicted log K_{ow} values are higher than 4.5 which indicates that these structures are potentially bioaccumulative. For the structures with a higher degree of isopropylation (e.g. penta- and hexa-isopropylated constituents) both models predict log K_{ow} values higher than 10 which indicates reduced bioaccumulation of these constituents of the Substance.

- Using these log K_{ow} values ECHA estimated for the mono-, di-, tri- and tetra-isopropylated TPP constituents BCF_{max} values of 25056-44806, 23421-48215, 1612-25548, and 70-4734 L/kg wwt, respectively. Correcting these BCF_{max} values for fish metabolism using the metabolism half-life values obtained from BCFBAF yields $BCF_{max, corr}$ values of 626-634, 4046-4440, 950-5688, and 70-4412 L/kg wwt for the mono-, di-, tri- and tetra-isopropylated TPP constituents, respectively. The applied fish metabolism half-life values are 1.8, 13.6, 6.5-104, and 49-197 days for the mono-, di-, tri- and tetra-isopropylated TPP constituents, respectively. The metabolism predicted for the mono isopropylated TPP constituents is faster than reported in the 90-day partial life-cycle toxicity discussed above (t1/2 <7 days). This adds to the uncertainty of the $BCF_{max, corr}$ value predicted for the mono-isopropylated TPP constituents, especially when considering that the experimentally determined BCF values for the mono-isopropylated TPP constituent of the Substance are much higher, ranging from 6133 to 9250 L/kg wwt. The QSAR predictions show that the di-, and tri-isopropylated constituent groups have the highest bioaccumulation potential.

Conclusion on the available information

The available information suggest that the mono-, di-, tri- and tetra-isopropylated TPP constituents of the Substance may have B/vB properties. Further information on the B/vB

properties may be requested in a follow-up decision making process in case one or more constituents meets the (screening) (v)P criteria.

c) [Potential] T properties

If a substance fulfils the criteria in Section 1.1.3 of Annex XIII to REACH, it is considered to fulfil the toxicity (T) criterion.

For the purpose of the assessment of T and to check whether the criteria are fulfilled, the information listed in Section 3.2.3 of Annex XIII must be considered.

Because the focus of the decision is on the P/vP properties, the existing information on the toxicity of the Substance is only shortly summarised following the evaluating MSCA's assessment.

Evidence based on experimental data

- The registration dossier of the Substance contains a fish early life-stage toxicity test according to OECD TG 210 for the commercial product Reofos [redacted]. Fathead minnows were exposed to mean measured concentrations of 1.3 to 51 µg/L under flow-through conditions for 33 days. The study reports a NOEC of 3.1 µg/L based on growth, and is expressed as mean measured concentration of the UVCB Reofos [redacted].

- The registration dossier of the Substance contains a *Daphnia magna* reproduction test according to OECD TG 211 for the commercial product Reofos [redacted]. The daphnids were exposed to mean measured concentrations of 6.77 to 268 µg/L under flow-through conditions for 21 days. The study reports a NOEC of 41.5 µg/L for daphnia based on reproduction and growth, which is expressed as mean measured concentration of the UVCB Reofos [redacted].

- The registration dossier of the Substance contains two algal growth inhibition tests according to OECD TG 201. The study with the commercial product Durad [redacted] showed a non-monotonic response and was considered unreliable. The study with the commercial product Reofos [redacted] was performed at nominal test concentrations of 0.16 to 2.5 mg/L for 72 hours. The study reports a NOEC of 0.31 mg/L based on growth rate and expressed as nominal concentration. Expressing this value as mean measured concentration of the UVCB Reofos [redacted], yields a NOEC of 47 µg/L.

- The UK-RER on isopropylated triphenyl phosphate reports additional long-term aquatic invertebrate toxicity tests from public literature using the commercial products [redacted] and Phosflex [redacted] (Sanders et al., 1985). Effect concentrations are expressed as mean measured concentration of the UVCB's:
  - *Daphnia magna*: NOECs of 6 µg/L ([redacted]; reproduction) and 28 µg/L (Phosflex 31P; survival and reproduction), as determined in a 21-day flow-through test at 6-154 µg/L Kronitex 200 and 0.85-56 µg/L Phosflex 31P, respectively.
  - *Gammarus pseudolimnaeus:* NOECs of 11 µg/L ([redacted]; survival) and 19 µg/L (Phosflex [redacted]; survival), as determined in a 90-day flow-through test at 0.5-128 µg/L [redacted] and 5-88 µg/L Phosflex [redacted], respectively.
  - *Chironomus plumosus*: NOECs of 184 µg/L ([redacted]; emergence) and 184 µg/L (Phosflex [redacted]; emergence), as determined in a 30-day flow-through test at 18-1500 µg/L [redacted] and 18-1500 µg/L Phosflex [redacted], respectively.

As all studies are conducted with the commercial products, they are not suited to provide (no) effect concentrations for the individual constituents. Therefore, while the lowest NOEC of 3.1 µg/L meets the T criterion, no conclusions can be drawn regarding the individual constituents.

The Substance is self-classified as Repr. 2 and STOT RE 2 (adrenal glands) irrespective of the TPP concentration being above or below 5%. This indicates that the mammalian T criterion might be met.

Conclusion on the available information

The available information suggests that the Substance may have T properties. Further information on the T properties may be needed in a follow-up decision-making process in case one or more of the constituents will meet the P and B criteria

1.2 Potential exposure

According to the information you submitted in all registration dossiers, the aggregated tonnage of the Substance manufactured or imported in the EU is in the range of 1000 – 10 000 tonnes per year.

Furthermore, you reported that among other uses, the Substance is used:

- in manufacture in closed or batch processes, with transfer of substance or mixture at dedicated and non-dedicated facilities and with hand-mixing with intimate contact with only personal protective equipment available during formulation;
- in industrial formulation into coatings, paints, adhesives, sealants, heat transfer fluids, laboratory chemicals and photo-chemicals, lubricant additives, greases and metal working fluids, and polymer mixtures;
- in coatings, paints, fire resistant foams, lubricants, lubricant additives, greases and metal working fluids, adhesives and sealants by professional workers;
- in coatings, paints, indoor functional fluids in machines and vehicles, lubricants and grease in vehicles, polymer mixtures, photo-chemicals, sealants and adhesives, fire resistant plastics and related products, fire resistant foam, and application of lubricant by dipping, brushing and spraying by consumers.

Therefore, exposure to the environment cannot be excluded.

1.3 Identification of the potential risk to be clarified

Based on all information available in the registration dossier and information from the published literature, there is sufficient evidence to justify that the Substance may be a PBT/vPvB substance.

The information you provided on manufacture and uses demonstrates a potential for exposure of the environment.

Based on this hazard and exposure information the substance poses a potential risk to the environment.

As explained in Section 1.1 above, the available information is not sufficient to conclude on the potential hazard and in particular on the vP/vP properties. Consequently, further data is needed to clarify the potential risk related to PBT/vPvB properties.

1.4 Further risk management measures

If the Substance is confirmed as meeting the P, B and T or vP and vB criteria it can be identified as a PBT/vPvB. The evaluating MSCA will analyse the options to manage the risk(s) and will assess the need for:

- further regulatory risk management in the form of identification as a substance of very high concern (SVHC) under Article 57 of REACH;
- a subsequent authorisation or a restriction of the Substance. This would result in stricter risk management measures than currently in place, such as minimisation of emissions, better waste management and revised instructions on safe use, if appropriate.

2. How to clarify the potential risk

2.1 Development of the testing strategy

As a first step, ready biodegradation tests are requested where the eleven specified mono-, di- and tri-isopropylated constituents of the Substance have to be tested separately. The evaluating MSCA will assess the information submitted by you, together with other available data, and will decide whether further information is needed to clarify the P/vP, B/vB, or T properties.
The ready biodegradation tests may allow to conclude that the tested constituents of the Substance are not P/vP, but they will not allow a definitive conclusion that they are P or vP. If a conclusion “not P/vP” cannot be drawn for the mono-, di- and tri-isopropylated TPP constituents, further testing (e.g. simulation testing) may therefore be needed to clarify the P/vP property, if necessary targeted to specific isomers. If the evaluating MSCA considers that further information is needed it will submit a new draft decision.

2.2 Ready biodegradability - test methods suitable for poorly soluble substances: CO_2 evolution test (OECD TG 301B), OR modified MITI(I) test (OECD TG 301C), OR manometric respirometry test (OECD TG 301F), OR CO_2 in sealed vessels (headspace test; OECD TG 310), with eleven selected constituents of the Substance.

a) Aim of the study

The aim of the study requested is to conclude whether the Substance screens as not P/vP or whether further testing is necessary to clarify the potential risk related to the PBT/vPvB properties.
The tests are requested based on the following considerations:

- The available biodegradation screening data on the Substance are equivocal. Ready biodegradation tests performed with commercial products that are associated with the Substance, reported mineralization in the range of 13 to 80% within 28 days. These test show that biodegradation of the Substance can occur under the conditions of a ready biodegradation test. However, considering that the commercial products consist for 4 to 35% of the biodegradable constituent TPP and that the level of isopropylation is not specified, it remains unclear to what extent individual isopropylated TPP constituents biodegrade, and how biodegradation is affected by the level of isopropylation.

- The tri-isopropylated TPP constituent tris[4-(1-methylethyl)phenyl] phosphate showed no mineralization within 28 days in a modified MITI(I) test. However, the test was conducted at a default test concentration of 100 mg/L, which greatly exceeds the predicted water solubility of 0.026 µg/L. It was not reported if the test material was dispersed. Consequently, it cannot be excluded that the lack of

biodegradation is the result of low bioavailability of the test substance.

- The mono-isopropylated constituent group of the Substance showed in a non-guideline water/ sediment degradation simulation study limited mineralisation after 28 days reaching a maximum of 8.4% of the applied radioactivity. Primary degradation was also reported to be low, with most of the radioactivity corresponding to the parent substance after 28 days. While the mono-isopropylated constituent group of the Substance appears to be poorly biodegradable, a definitive conclusion on P/vP could not be reached as reliable DT50 could not be derived and there were too many uncertainties in the study including the viability of the sediment.

A ready biodegradability test (e.g., OECD TG 301) is a standard information requirement at Annex VII, Section 9.2.1.1 of REACH. It could therefore be subject to a compliance check under Article 41 of REACH. However, the current study request is to clarify the degradability of specific constituents of the Substance and will therefore not be performed on the registered Substance but instead on test materials representative of the mono-, di-, and tri-isopropylated TPP constituent groups of the Substance. Also, several additions to the standard test guideline are required, such as modifications to improve the bioavailability of the test substances and testing the test substances separately. Since non-standard parameters are required and the information request is based on a potential risk that the Substance poses, the request is necessary under the current substance evaluation.

In your comments to the draft decision you note that different ready biodegradation test methods are suitable to study the biodegradability of poorly water-soluble compounds, and that it should be at your discretion to determine the method to be used. You argue that the specified test methods, i.e. MITI(I) test (OECD TG 301C) and Manometric Respiratory test (OECD TG 301F) are conservative in determining the ready biodegradability of poorly water-soluble substances in comparison to other suitable methods, i.e. the CO_2 evolution test (OECD TG 301B) and CO_2-Headspace test (OECD TG 310). You underpin this statement by referring to an ongoing thesis ([redacted], 2021), as well as to peer-reviewed public literature studies (Dick et al., 2016; Kayashima et al., 2014).

- The thesis investigated 134 substances with a water solubility of <1 mg/L whose ready biodegradability was assessed in an OECD ready biodegradability test. You concluded that the percentage substances reaching the pass level amounted to 5% (1 of 19), 15% (5 of 34), 36% (19 of 53) and 67% (2 of 3) in an OECD TG 301C, 301F, 301B and 310 study, respectively. ECHA notes that the thesis was not available to ECHA. As it remains unclear whether the underlying data are reliable, suitable and exhaustive, the outcome of the thesis cannot a priori be relied upon.
- Regarding the public literature studies, Dick et al. (2016) concluded that OECD TG 301C is conservative in comparison to OECD TG 301F and that lowering of the initial test concentration in combination with extending test duration increases the level of biodegradation. Kayashima et al. (2014) showed that OECD TG 301C is conservative in comparison to OECD TG 301A, 301B, 301D, 301E, 301F and 310 for, amongst others, phosphorus compounds, most likely due to the particularity of its inoculum. The reference Seyfried et al. was not further detailed in your comments and as it could refer to several publications, it is not further discussed here.

ECHA notes in addition to the above public literature, that the UBA report “Assessment of environmental persistence: regulatory requirements and practical possibilities – available test systems, identification of technical constraints and indication of possible solutions“

(Gartiser et al., 2017) ranked the potency (biodegradation potential) of ready biodegradation studies as follows: (****) OECD TG 301B; (***) OECD TG 301F and 310; and (**) OECD TG 301C. Considering the above, as well as ECHA Guidance Chapter R.7b, ECHA acknowledges that while the MITI(I) test method (OECD TG 301C) is suitable to test poorly water-soluble substances, it appears to be more conservative than the other three suitable methods (OECD TG 301B, 301F and 310). There are no indications that the same would apply to OECD TG 301F where the inoculum treatment does not deviate from the other two methods suitable for poorly water-soluble substances (i.e. OECD TG 301B and 310).

The evaluating MSCA specified initially the test methodology as being OECD TG 301C or 301F, because the use of OECD TG 301B (CO_2 production) is considered less optimal to ensure maximal bioavailability of the test substance to the inoculum. OECD TG 301B requires aeration and hence (especially for the higher isopropylated isomers) the test material can possibly be forced out of the biological test system before degradation takes place. Although volatility is not directly expected to complicate the testing of the specific isopropylated TPP isomers, it is a confounding factor to take into account. The OECD TG 310 (CO_2 headspace analysis) is available as an update of the OECD TG 301B test methodology, and could therefore be a more suitable alternative as it would exclude false negative results due to volatilization.

Considering the above, the request has been adapted allowing you to determine which of the above discussed suitable methods you will use to assess the ready biodegradability of the selected constituents.

b) Specification of the requested study

Test material

The tests must be conducted with the specified mono-, di-, and tri-isopropylated TPP constituents of the Substance. These constituents represent the constituent groups with the highest potential for PBT/vPvB properties, based on their apparent bioaccumulation potential indicated by the QSAR analyses.

The specified mono-, di-, and tri-isopropylated TPP constituents of the Substance have isopropyl groups on different positions on the phenol ring and/or are differently distributed over the rings. Biodegradability data on these substances will allow to draw conclusions for constituents within the same constituent group that have not been tested. Additionally, these data might also allow to conclude on the potential P/vP properties of tetra-isopropylated TPP constituents that have not been included in this decision, but that also screen as potentially bioaccumulating based on QSAR analyses.

In your comments to the draft decision you noted that based on QSAR profiling the di- and tri-isopropylated TPP constituent groups of the substance have the highest potential for PBT/vPvB properties and you do not see a reasonable risk that the mono-isopropylated TPP constituents would evolve from experimental testing with a higher concern for P or B. Therefore, you deem testing representative di- and tri-isopropylated TPP constituents sufficient, also taking the aspect of proportionality into account. ECHA agrees that the highest PBT/vPvB concern is indeed for the di-, and tri-isopropylated TPP constituents of the Substance. However, the mono-isopropylated TPP constituents of the Substance are also predicted as PBT substances. Furthermore, for this group of substances experimental data suggest that P/vP criteria may be met in the sediment (Heitkamp *et al.*, 1984), while the fish bioaccumulation study strongly suggests that one or more constituents of the mono-isopropylated TPP group of the Substance are B/vB. Overall, it is necessary to conclude on the persistence of the mono-isopropylated TPP constituents, in order to

exclude any uncertainties left with respect to the PBT/vPvB properties of these constituents. Omitting testing of any of the selected constituents, such as mono-isopropylated TPP, may lead to additional testing at a later stage, causing delay in clarifying the P/vP properties. In addition, the evaluating MSCA considers that testing all the selected constituents separately in the same study, with the same inoculum and under the same test conditions, gives a better basis for comparing their degradability and thus for selecting the appropriate test material for further testing, if necessary. The request has not been adapted.

Requirements for inoculum

You are requested to sample the inoculum for the ready biodegradation tests with the eleven selected constituents from a municipal sewage treatment plant (STP) in a more rural area to minimize the occurrence of inoculum (pre-)adapted to the test substance(s). You should justify the decision for the sampling site by providing further information about the sewage treatment plant the inoculum was taken from. This has to include information such as the location, STP treatment capacity, number of inhabitants connected, and sampling date.

Modifications and enhancements to improve bioavailability

The water solubility of the mono-, di-, and tri-isopropylated TPP constituents of the Substance is estimated to be 26, 0.83 and 0.026 µg/L, respectively (WSKOW). You must take measures to improve the bioavailability of the test substances to overcome solubility issues associated with the Substance. Suitable methods include dispersal by ultra-sonification, dispersal on silica gel/glass beads and use of silicone oil. As specified in REACH guidance R7b, the use of silica gel matrices is generally seen as the preferred option (ECHA, 2017). More guidance on how to evaluate the biodegradability of poorly soluble substances is given in Annex III of the OECD TG 301, where it is indicated that sufficient, but not excessive, agitation during testing may be used to keep the substance dispersed. When OECD TG 301C is followed, solvents or emulsifying agents should not be used. It is advised to optimize the modifications before testing all specified constituents.

In your comments to the draft decision, you noted that you want to test different modifications to improve bioavailability of the substances, as well as other enhancements (larger test vessels and prolonged test duration) in a consecutive manner, to be able to take learnings into account for follow-up tests. As discussed below, prolonging the test duration is not deemed warranted, while using larger test vessels may be applied. ECHA considers that the modifications to improve bioavailability and the application of larger test vessels can be tested simultaneously. This will reduce the time needed for testing, while at the same time the comparability of different tests will be facilitated as the inoculum will not differ between treatments. Based on these preliminary tests you can determine the most suitable testing conditions for the definitive ready biodegradability tests to be conducted. The outcome of the definitive tests, but also the preliminary tests, should be included in the updated REACH registration dossier, so ECHA can evaluate if the chosen conditions are indeed adequate. ECHA considers that the allocated time is sufficient for such a test setup.

Modifications to improve bioavailability are preferred above prolonging test duration when investigating the biodegradability of poorly-water soluble substances (ECHA, 2017a). The guidance further notes that prolongation of the test duration should only be considered if some initial, slow but steady, biodegradation was observed but did not reach a plateau by the end of the ready biodegradability test, i.e. after 28 days. The available modified MITI(I) test with the tri-isopropylated TPP constituent tris[4-(1-methylethyl)phenyl] phosphate

showed no biodegradation at all within 28 days. Considering all, the duration of the ready biodegradation tests must not be extended beyond 28 days.

In your comments to the draft decision, you argue that it should be at your discretion to proceed as currently requested (i.e. apply modifications to improve the bioavailability) or, alternatively, enhance the tests by extending the test duration to a maximum of 60 days or use larger test vessels. You refer to the same guidance text as did ECHA in the paragraph above noting that a prolonged test duration is only meaningful when "some initial, slow but steady, biodegradation observed within 28 days not having reached a plateau". ECHA already noted that modifications to improve bioavailability are preferred instead of prolonging the test duration, when investigating the biodegradability of poorly-water soluble substances and that the currently available data for the tri-isopropylated TPP constituent tris[4-(1-methylethyl)phenyl] phosphate does not demonstrate the degradation pattern to which you referred. For these reasons, the extension of the test duration is not justified.
Furthermore, a degradation result from an enhanced biodegradation screening test cannot be used to conclude on the ready biodegradability of a substance (ECHA, 2017a), and can only be used to conclude "not P or vP" if there is other supporting information available. Guidance Chapter R.11 on the PBT/vPvB assessment remarks: "*Positive results from enhanced screening tests may be used together with other supporting information to conclude that the substance is not P/vP*" (ECHA 2017b), but this would require an interpretation of expected rate of degradation in the test. Contrarily, the results from ready biodegradability tests, with or without modifications to improve bioavailability, allow to conclude on the ready biodegradability. The outcome of the latter tests can thus be directly compared to the P screening criterion, yielding conclusive data. Data generated with enhanced biodegradation screening tests that have an extended test duration may not be clear-cut (e.g. is extension warranted and did adaptation of microorganism occur). Consequently, simulation degradation testing may possibly still be needed to conclude on the persistence of some of the constituents.

In addition, as extending the test duration is an enhancement to account for the reduced bioavailability in the test, it cannot be combined in the same test with modifications to improve the bioavailability, such as silica gel. Therefore, extended test duration would require separate testing, which is neither considered necessary nor proportional as it would not be expected to provide any necessary information in addition to that obtained from ready biodegradation tests with modifications to improve bioavailability. The other proposed enhancement, i.e. larger test vessels, is not intended to improve bioavailability, but to increase the likelihood of introducing microorganisms that can metabolize the test substance. It is therefore considered appropriate to combine it with the modifications to improve bioavailability, and the data are likely sufficiently robust to allow concluding that the test substances are not P and not vP or that they are potentially P or vP (even though the data cannot serve to conclude on the ready biodegradability of the test substances).

Overall, as the aim of this decision is to determine whether further simulation testing is needed for one or more constituents of the Substance based on conclusive data from screening level studies, the current request has only been adapted to allow the use of larger test vessels.

Consideration of time needed to perform the requested studies

In your comments to the draft decision you requested an extension of the time needed to perform the requested studies to 24 months based on the following justifications:

- Test material: you noted that based on an initial assessment, all of the specified mono-, di-, and tri-isopropylated TPP constituents of the Substance may not be readily available for purchase. You indicated that further exploration of whether the substances in question are commercially available must be undertaken. You have not however provided any documentary evidence from the test material providers to support this claim. Therefore, at this moment, there is no evidence to justify an extension of the deadline.
  However, ECHA recognises the potential availability issue and provides an alternative timeline of 12 months, upon the condition that you can sufficiently demonstrate, via documentary evidence of an exhaustive search and of correspondence with the test material providers, that all specified test constituents are not commercially available. In such a situation you would be required to synthesize the respective materials and test them accordingly. ECHA considers that an additional 6 months is sufficient for synthesising the commercially unavailable constituents.
- Improving bioavailability and increasing test vessels size: you propose to test different modifications to improve bioavailability, as well as other enhancements in a consecutive manner. As explained in the section above, ECHA considers that the modifications and application of larger test vessels can be tested simultaneously and therefore do not sufficiently justify an extension of the deadline.
- Test duration: You propose to modify the tests by extending the test duration to a maximum of 60 days. As explained above, ECHA considers that an extension of the test duration is not warranted. Consequently, an extension of the deadline on this basis is not justified.

Consequently, the deadline for submission of the requested information has not been amended as such.
However, if you can provide documentary evidence of an exhaustive search and correspondence with the test material providers supporting your claim that the specified test constituents are not all commercially available, the timeline for submission of the requested information is extended to 12 months from the date of the decision, to allow sufficient time for the synthesis of these constituents.

In your comment to the received proposals for amendment (PfA) you once more noted that 24 months are needed to comply with the request, as apparently only one of the substances is commercially available from the two test material providers you inquired with. ECHA notes that while your comment is not directly linked to the referenced PfA, it was considered for the sake of transparency. It is noted that you initially requested 24 months not only to synthesise the test material, but also to allow sequential testing and testing of prolonged test duration. ECHA notes that your comments to the PfA now request the same time period for the synthesis of test material only. You did however not provide any further evidence that justifies altering the time already provided in the draft decision, except your awareness that the substances are difficult to synthesize.

The draft decision was therefore not further adapted with respect to the deadline. In your comments you also indicate that it remains unclear what type of documentary evidence is to be provided to ECHA in case the test material cannot commercially be obtained. ECHA therefore adapted the draft decision and further specified which evidence would be considered as acceptable to justify an application of an extended, alternative timeline of 12 months.

Request for the full study report

You must submit the full study report which includes:

- a complete rationale of test design and
- interpretation of the results of preliminary and definitive tests
- access to all information available in the full study report, such as implemented method, raw data collected, interpretations and calculations, consideration of uncertainties, argumentation, etc. of both preliminary and definitive tests.

This will enable the evaluating MSCA to fully and independently assess all the information provided, including the statistical analysis, and to efficiently clarify the potential hazard for the PBT/vPvB properties of the Substance.

c) Alternative approaches and how the request is appropriate to meet its objective

The request is:

- Appropriate, because the test is suitable and necessary to obtain information which will allow clarifying whether the mono-, di-, and tri-isopropylated constituents of the Substance fulfil the screening criterion for P/vP and thus whether further information would still be needed to clarify the P/vP property. Additionally, the requested data is expected to indicate the worst-case constituents to be selected when further testing is needed.
- The least onerous measure, because by conducting a ready biodegradability test, the need for simulation testing will be avoided in case a conclusion that all constituents of the Substance are not P/vP can be drawn.

2.3 References relevant to the requests (which are not included in the registration dossier)

Brooke D.N., Crookes M.J., Quarterman P., and Burns J. (2009). Environmental risk evaluation report: Isopropylated triphenyl phosphate (CAS nos. 28108-99-8, 26967-76-0 & 68937-41-7). Product code: SCHO0809BQUG-E-P. Environment Agency, Bristol, UK.

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ECHA (2017a). Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7b: Endpoint specific guidance. (version 4.0, June 2017). Appendix R7.9-3.

ECHA (2017b). Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.11: PBT/vPvB assessment. (version 3.0, June 2017).

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National Institute of Technology and Evaluation (1984a). Biodegradation in water: screening test for tris(4-isopropylphenyl) phosphate (CAS no.: 2502-15-0; MITI number 3-2534). Published in: Official Bulletin of the Japanese Ministry of International Trade and Industry. Accessed: 15-01-2021. https://www.nite.go.jp/chem/jcheck/tempfile_list.action?tpk=22472&ppk=4663&kinou=100&type=ja

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Sanders H.O., Hunn J.B., Robinson-Wilson E.R., and Mayer F.L. (1985). Toxicity of seven potential polychlorinated biphenyl substitutes to algae and aquatic invertebrates. *Environmental Toxicology and Chemistry*, 4, 149-154.

Appendix B: Procedure

This decision does not imply that the information you submitted in your registration dossier(s) are in compliance with the REACH requirements. ECHA may still initiate a compliance check on your dossiers.

12-month evaluation

Due to initial grounds of concern for PBT/vPvB and for endocrine disruption, the Member State Committee agreed to include the Substance (EC No 273-066-3, CAS RN 68937-41-7) in the Community rolling action plan (CoRAP) to be evaluated in 2020. The Netherlands is the competent authority ('the evaluating MSCA') appointed to carry out the evaluation.

In accordance with Article 45(4) of REACH, the evaluating MSCA carried out its evaluation based on the information in the registration dossier(s) you submitted on the Substance and on other relevant and available information.

The evaluating MSCA completed its evaluation considering that further information is required to clarify the following concerns: PBT/vPvB.

Therefore, it submitted a draft decision (Article 46(1) of REACH) to ECHA on 30 August 2021.

Decision-making

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

For the purpose of this decision-making, dossier updates made after the date the draft of this decision was notified to you (Article 50(1) of REACH) will not be taken into account.

(i) Registrant(s)' commenting phase

ECHA received your comments and forwarded them to the evaluating MSCA. The evaluating MSCA took your comments into account (see Appendix A). The request(s) and the deadline were amended.

Amendment of the deadline(s)

In your comments to the draft decision, you requested an extension of the timeline from 6 months as indicated in the draft decision to 24 months. ECHA has not modified the deadline of the decision, but provided a conditional, alternative timeline of 12 months, as specified in the section '*Consideration of time needed to perform the requested studies*'.

(ii) Proposals for amendment by other MSCAs and ECHA and referral to the Member State Committee

The evaluating MSCA notified the draft decision to the competent authorities of the other Member States and ECHA for proposal(s) for amendment.

Subsequently, the evaluating MSCA received proposal(s) for amendment to the draft decision and modified the draft decision (see Appendix A, B or C).

ECHA referred the draft decision, together with your comments, to the Member State Committee.

ECHA invited you to comment on the proposed amendment(s). Your comments on the proposed amendment(s) were taken into account by the Member State Committee. In addition, you provided comments on the draft decision.

(iii) MSC agreement seeking stage

The Member State Committee reached a unanimous agreement in its MSC-76 written procedure and ECHA took the decision according to Article 52(2) and Article 51(6) of REACH.

After the deadline set in this decision has passed, the evaluating MSCA will review the information you will have submitted and will evaluate whether further information is still needed to clarify the potential risk, according to Article 46(3) of REACH. Therefore, a subsequent evaluation of the Substance may still be initiated after the present substance evaluation is concluded.

Appendix C: Technical Guidance to follow when conducting new tests for REACH purposes

Test methods, GLP requirements and reporting

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.

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.

Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[2].

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*

   a) 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.
   b) The reported composition must include all constituents of each Test Material and their concentration values

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 "How to prepare registration and PPORD dossiers"[3].

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