Helsinki, 14 June 2021

Addressees
Registrant(s) of Methylethylketone peroxide trimer listed in the last Appendix of this decision

Registered substance subject to this decision (the Substance)
Substance name: Methylethylketone peroxide trimer
EC number: 429-320-2
CAS number: 24748-23-0

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. Simulation testing on ultimate degradation in surface water (test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25. /OECD TG 309) on the Substance, performed as follows:

- as a pelagic test (i.e. surface water with a natural content of ~15 mg suspended particulate matter (SPM) dw/L);
- at an environmentally relevant temperature of 12 °C;
- the concentration of the methylethylketone (MEK) peroxide trimer main constituent must be measured at appropriate intervals during the study so that a reliable primary degradation half-life can be determined;
- the transformation and/or degradation products relevant for PBT/vPvB assessment or for obtaining a mass balance of MEK peroxide trimer must be identified and quantified;
- the test set-up must enable to check the mass balance of the methylethylketone (MEK) peroxide trimer main constituent in the Substance;
- if non-labelled test material is used, sterile purified water controls must also be included in the test;
- minimising any losses of the MEK peroxide trimer due to volatilisation or sorption, and/or accounting for these processes in a closed mass balance;
- the amount of non-extractable residues (NER) must be quantified and you must include a scientific justification of the extraction procedures and solvents used, as far as technically feasible.

You are requested to report back the results and interpretation from the information Request A.1 to the eMSCA in order to decide whether Request A.2 is necessary.

Only if the result from Request A.1 shows an environmental half-life exceeding 40 days in the aquatic aerobic compartment (according to the P-criterion in Annex XIII to REACH),

Or

Only if it is not (technically) feasible to derive a reliable environmental half-life after simulation testing according to OECD TG 309, and where the technical difficulties are properly justified,

Then the following study is requested:

2. **Bioaccumulation test in aquatic species (test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD TG 305) on the Substance, performed as follows:**
   - via aqueous exposure;
   - the excessive fish growth and lipid increases must be avoided, since these might confound the results;
   - the results must be corrected for growth and normalized to 5% lipid content;
   - the test must be conducted in a flow-through system;
   - the exposure concentrations must be monitored during the experiment;
   - The BCF of the MEK peroxide trimer main constituent in the Substance must be measured.

Deadlines

A sequential testing strategy is therefore applied with multiple deadlines, as set out below.

Table 1 - Requested studies and corresponding deadlines

Requested information	**Conditions when to perform test**	**Deadline**
Request A.1: Persistence in the aerobic aquatic environment	None – must always be performed	**19 June 2023** This includes: 18 months to finalise and report the results of the Request A.1 to the NL competent authority; and 3 months for dossier update and to agree with the NL competent authority how to proceed with Request A.2.
Request A.2: Bioconcentration factor in aquatic species	Only if the result from Request A.1 shows an environmental half-life exceeding 40 days or only if it is not (technically) feasible to derive a reliable environmental half-life from Request A.1 (with proper justification)	**14 December 2023**

ECHA
EUROPEAN CHEMICALS AGENCY

Conditions to comply with the information requested

To comply with this decision, you must submit the information in an updated registration dossier, by the deadlines indicated above. The information must comply with the IUCLID robust study summary format. You must also attach the full study report for the corresponding study/ies 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 A 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] by Laurence Hoffstadt, Team leader of Substance evaluation

[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 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

1. Potential risk

1.1 Potential hazard of the Substance

The PBT concern is raised due to the presence of methylethylketone (MEK) peroxide trimer, which is the main constituent of the registered Substance: [redacted]% w/w of the Substance, dissolved in petroleum distillates (EC number 265-149-8, CAS RN 64742-47-8). Following its assessment of the available relevant information on the Substance, the evaluating MSCA and ECHA have identified that the potential hazards are specific to the methylethylketone (MEK) peroxide trimer (constituent of the Substance) and must be clarified.

Annex XIII to REACH provides that the identification of PBT/vPvB substances must also take account of the PBT/vPvB properties of relevant constituents. According to ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.11: PBT/vPvB assessment (June 2017, Section R.11.4.1), a constituent should normally be considered relevant for the PBT/vPvB assessment when present in a concentration of ≥ 0.1% (w/w). For the PBT assessment of the Substance, the evaluating MSCA considers that the MEK peroxide trimer constituent is relevant because it is present at about [redacted]% concentration. The PBT concern focusses on the main constituent MEK peroxide trimer.

a) [Potential]P/vP properties

The available information suggests that the Substance may be persistent in the environment.

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.

The Substance fulfils the screening criteria for Persistence, according to the experimental test data in your registration dossier and to additional (QSAR) information generated by the eMSCA:

- An OECD TG 111 test (Hydrolysis as function of pH) (2014) shows an hydrolysis half-life of 22.7 hours at pH 7 and 12°C. Also at pH 4 and 9 the half-life is close to 1 day. These results are contradicting the available biodegradation test results, as well as hydrolysis test results from registration dossiers of structural analogues (other organic peroxide polymerization starters).
- A higher tier OECD TG 111 test (with identification of hydrolysis products, Tier 3) was performed in 2017, after the eMSCA questioned the hydrolysis results reported in the previous test (2014). No significant hydrolysis products were detected during the course of this 90-day study. The presence of organic material, addition of an iron complex or elevating the temperature had no effect on the stability of the test substance. The main constituent MEK peroxide trimer is therefore not expected to undergo any hydrolysis in the environment.
- An OECD TG 301B test (Ready Biodegradability: CO2 Evolution Test) (unnamed study report, 1997) with the Substance shows 9% mineralization (CO_2 generation)

after 28 days, indicates that the Substance (and its main constituent MEK peroxide trimer) is not readily biodegradable.

- An OECD TG 301D test (Closed Bottle Test) (unnamed study report, 2001) shows 3% mineralization (oxygen consumption) after 28 days, confirming the result from the OECD TG 301B test. This test has however been extended, reaching 13% mineralization after 56 days, 59% after 120 days and ultimately 65% after 140 days. You concluded that the Substance is therefore inherently biodegradable. However, extending the test to a duration of 140 days gives results that are difficult to interpret, and is considered not acceptable by the eMSCA. It should be noted that a ready biodegradability test, even if extended to 140 days, cannot be used to conclude on the environmental half-life or the fulfilment of the P-criterion for the P-assessment.
- An OECD TG 302B test (Inherent biodegradation test, Zahn-Wellens) (unnamed study report, 2018) has been performed, with active measurement of the hypothesized first degradation product of the hydrolysis of the peroxide bond in the Substance, MethylEthylKetone (MEK). However MEK was not detected when testing the Substance. You concluded that the Substance is therefore not removed by alkyl hydroperoxide reductases in the Zahn-Wellens test, and that the Substance is not inherently biodegradable in this test. The eMSCA concludes that the main constituent MEK peroxide trimer in the Substance is therefore not inherently biodegradable.
- Under additional information in the Summary of the Biodegradation in water: Screening tests, you stated "*Studies with a mixture of organic peroxide (CAS [redacted]) with the registered substance as main constituent showed similar results. This mixture was not found readily biodegradable and neither inherently biodegradable.*" CAS RN [redacted] is a mixture of MEK peroxide trimer and the close structural analogue Methyl Propyl Ketone (MPK) peroxide trimer in petroleum destillates as stabilizer.
- QSAR estimations of the environmental (aquatic) biodegradability for the MEK peroxide trimer using the US EPA BioWIN v4.10 models give the following results:
    - Ready biodegradability (BioWin5 and 6 models): Not readily biodegradable
    - Inherent biodegradability (BioWin 1 and 2 models): Biodegrades slowly in the environment
    - Ultimate degradation survey (BioWin 3 model): half-life of months for ultimate degration, the model result of 1.9787 is also well below the screening criterion of 2.2 used in the REACH Guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment, indicating (potential) P or vP properties of a substance.
- Furthermore, it is unclear if the test results in some of the tests mentioned above reflect degradation of the Substance, which is a solution of the constituent methylethylketone peroxide trimer ([redacted]% w/v) in petroleum distillates ([redacted]%), or if it indicates degradation of the main constituent MEK peroxide trimer. The contribution of the solvent on the test results, e.g. in the extended OECD TG 301D described above, is therefore unclear. Since the constituents of petroleum distillates are known to be readily or inherently biodegradable results from both ready biodegradability tests as well as the inhererent biodegradability test will potentially give an overestimation of the percentage mineralization of the methylethylketone peroxide trimer. Overall, based on the weight of evidence of the available data the main constituent of the Substance, MEK peroxide trimer, is considered not readily nor inherently biodegradable.

As indicated in the ECHA Guidance R.11 (page 51) degradation simulation studies performed under environmentally realistic conditions are in principle the only tests that can provide a definitive degradation half-life for comparison with the criteria in Section 1.1.1 or 1.2.1 of Annex XIII to REACH.

Finally you are requested to report back the results and interpretation from the information request A.1 to the eMSCA in order to decide whether continued testing for B/vB properties is necessary.

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 that it has 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.
The available information suggests that MEK peroxide trimer may be bioconcentrating in aqueous organisms, possibly fulfilling the B-criterion for substances with PBT-properties as specified in Annex XIII to REACH.
MEK peroxide trimer fulfils the screening criteria for Bioaccumulation according to the test data in your registration dossier and to additional data from the eMSCA:

- An OECD TG 117 (Partition Coefficient (n-octanol / water), HPLC Method) yields an octanol water partition coefficient (log K_{ow}) of the MEK peroxide trimer of 4.84. This result is above the screening criterion for 'B' of 4.5 indicated in the REACH Guidance document R.11.
- An approximate experimental estimate of the log K_{ow} using the ratio of the measured water and octanol solubility (performed as a pilot for the OECD TG 117 test) gave a value of >4.3, using a water solubility of 26.9 mg/l and an octanol solubility of $>5x10^5$ mg/l. It is noted that when the actual water solubility from the key study in the registration dossier of 13.1 mg/l is used in this approximation, this approach results in an estimated log K_{ow} value of >4.60.
- QSAR estimates by the eMSCA for the MEK peroxide trimer give similar or higher estimates for the log K_{ow}. The publicly available KowWIN estimation program from the US EPA predicts a value for the MEK peroxide trimer of log Kow of 6.1. The estimate from the licensed ClogP software (Daylight Inc.) gives an estimate of 4.60 for the MEK peroxide trimer.
- A QSAR estimate of the BCF value for the MEK peroxide trimer using the US EPA BCFBAF v3.01 model gives an estimate of 4940 L/kg, very close to the vB criterion of 5000.

All available data show that the MEK peroxide trimer, main constituent of the Substance, exceeds the screening criterion for Bioconcentration (log K_{ow} > 4.5) as given in REACH Guidance R.11.

The available and current information is not sufficient to draw a conclusion on the hazard – potential bioconcentration. Further information is needed on the bioconcentration behaviour of the MEK peroxide trimer in the Substance in aquatic species, via aqueous exposure as this information is currently lacking in the dossier.

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, such as results of long-term toxicity tests. Also screening information of Section 3.1.3 to Annex XIII, such as short-term aquatic toxicity and QSAR predictions, should be considered in a weight-of-evidence approach to clarify the potential risk related to toxicity of the Substance.

Evidence based on experimental data

You have submitted short-term aquatic toxicity tests with fish (OECD TG 203), Daphnia (OECD TG 202) and algae (OECD TG 201), and a chronic toxicity test with daphnids (OECD TG 211) which applied water accommodated fractions (WAF) of the Substance. The acute tests showed no toxic effects up to total concentrations of the Substance of >1.4->4.32 mg/L. The chronic daphnid test showed no effects on reproduction up to the measured WAF concentration of the Substance of 2.7 mg/L. The LOEC at the next dose level (4.9 mg/L) already showed 90-100% mortality of the (parent) daphnids in the test. The results are considered to be unsuitable for PBT assessment of the MEK peroxide trimer constituent because concentrations of this consitituent in the WAF is not measured, concentration losses of the Substance in the acute toxicity fish test are high (56…65%) and WAF testing (chronic daphnid) is not considered appropriate for risk assessment purposes in general[2].

Evidence based on model predictions

The eMSCA applied the neutral organic ECOSAR (v1.11) QSAR model to the MEK peroxide trimer to get estimate of the expected baseline (minimum, or narcosis type) aquatic toxicity of this constituent. This results in chronic toxicity values (ChV) (algae) of 0.081 mg/L, ChV (Daphnid) 0.010 mg/L and ChV (fish) 0.007 mg/L for MEK peroxide trimer. The lowest ChV values for baseline toxicity for daphnid (0.010 mg/L) and fish (0.007 mg/L) are at or below the T criterion for long-term aquatic toxicity (NOEC < 0.01 mg/L).

The available acute and chronic aquatic toxicity tests with the Substance show little or no effects up to ~2 mg/L, given as the maximum solubility in the acute tests. In the WAF applied in the chronic daphnid tests the reported measured concentrations of the substance are up to 8.3 mg/L. The absence of effects at or below 2.7 mg/L (WAF of the Substance) in the chronic daphid test contrasts with the ECOSAR QSAR predictions (assuming base-line or narcosis type aquatic toxicity) for the constitutent MEK peroxide trimer. Furthermore, testing for aquatic toxicity is not complete as a long term fish toxicity test is not available.

The available and current information is not sufficient to draw a conclusion on the potential hazard. Further information on the T property might be requested in a follow-up decision making process if needed to clarify the potential risk related to the PBT/vPvB properties.

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 100 – 1000 tonnes per year.

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

- Manufacture (ERC1);
- Formulation into a mixture (ERC2);
- Industrial use of organic peroxides as polymerization initiators, cross-linking agents or curing agents (ERC 6b and 6d) with multiple opportunities for exposure.

[2] REACH guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment, Version 3.0, June 2017, Section R.11.4.1.3.5

The emission estimates you provided in the Chemical Safety Report indicate significant emissions to the freshwater compartment and the atmosphere, from manufacture, formulation and industrial use.

Furthermore, environmental monitoring data on comparable organic peroxide polymerization starters (Thomas *et al.*, 2014, 2015) show that these substances (with the same chemical functionalities and the same uses) occur in the environment, and are thus likely to be released untransformed from the final products (polymer matrices) they are used in.

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 MEK peroxide trimer, main constituent of the Substance, may be a PBT/vPvB substance.

The information you provided on emission from manufacture, formulation and industrial use of the Substance 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, the available information is not sufficient to conclude on the potential hazard and in particular PBT/vPvB. Consequently further data is needed to clarify the potential risk related to PBT/vPvB properties.

1.4 Further risk management measures

If the vPvB properties(s) of the Substance are confirmed, the evaluating MSCA will analyse the options to manage the risk(s). If the main constituent of the Substance is considered P and B, but not vP and vB, further testing might be required to draw a definitive conclusion on the T status of the substance. Further information requests could be formulated in a subsequent substance evaluation or compliance check based on the outcome of the information generated in the current substance evaluation.

New regulatory risk management measures could be identification as substance of very high concern (SVHC) of the Substance for PBT or vPvB properties and, as a consequence, improved measures at manufacturing sites, 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 explained in Section 1.1 above, MEK peroxide trimer is a relevant constituent of the Substance and testing aims to clarify its P and B properties. If this constituent is identified as PBT or vPvB, then the Sustance itself can be identified as such.

Request A.1 will provide information on the P/vP properties of the MEK peroxide trimer and the identity of any transformation and/or degradation products relevant for the PBT/vPvB assessment. The information from Request A.2 is required only if the results from Request 1 demonstrate that the MEK peroxide trimer fulfils the criteria for persistence (P) or very persistence (vP) according to Annex XIII to REACH, Section 1.1.1 or 1.2.2., or when it is (technically) not feasible to derive an environmental half-life for the Substance from Request A.1 and where the technical difficulties are properly justified. Request A.2 will provide information on the B/vB properties of the Substance.

The studies requested are standard information requirements of Annex IX to REACH which could be subject to a compliance check under Article 41 of REACH. However, because adaptations to the standard testing and GLP are being considered, substance evaluation is an appropriate process, also given that the information requested aims at clarifying the potential risk that the Substance poses. In addition, you have registered the Substance at the Annex IX level, which means that using the substance evaluation does not affect your rights or obligations as compared to compliance check.

2.2 Simulation testing on ultimate degradation in surface water

a) Aim of the study

Information on environmental persistence is required to conclude whether the MEK peroxide trimer constituent of the Substance fulfils the P-criterion under REACH.
Therefore a study is required that simulates environmental conditions and yields a result (a half-life in days under environmental conditions) that can be compared to the P-criterion. An OECD TG 303A test, and/or simple anaerobic degradation testing as proposed by the registrant as additional testing, may contribute to the overall Weight of Evidence conclusion on persistence in the environment, but results from the proposed tests cannot replace the requirement for simulation testing, also because the substance shows a high persistency in the available aerobic ready biodegradation, extended ready biodegradation and inherent biodegradation tests.

It is not intended to receive information on biodegradation behavior of the petroleum stabilizer but of the main constituent, MEK peroxide trimer.

Testing in water is considered appropriate for the following reasons:

- the aquous fresh water compartment is the most relevant compartment where emissions will occur according to the emission estimates in the Chemicals Safety Report;
- Level III fugacity model as implemented in the EPISuite software from US EPA shows that a significant amount of the emissions remains in the aquatic compartment.
- Based on the physico-chemical properties of the main constituent of the Substance (water solubility, volatility, octanol-water partition coefficient) simulation testing for the aquous compartment is considered feasible.

Substance evaluation is the appropriate process to request further data as there is a potential risk based on the registration dossier data as well as additional information acquired by the evaluating MSCA (QSAR-modelling and exposure monitoring; sections 1.1 and 1.2.
In addition, the study (OECD TG 309) is requested with necessary modifications (monitoring of a specific constituent) to the standard design to ensure that information related to a constituent of concern is provided.

b) Specification of the requested study

Test material and concentration

The test shall be performed with the Substance, but you must report the mass balances specifically for the constituent MEK peroxide trimer. In case this is for justified technical reasons not possible, the following alternative is acceptable: testing with MEK-peroxide trimer alone, or testing a mixture of MEK- and MPK-peroxide trimer, as present in the

REACH registered substance 1,2,4,5,7,8-Hexoxonane, 3,6,9-trimethyl-, 3,6,9-tris(Ethyl and Propyl) derivatives (upper limit: 41% w/w; typical concentration: [redacted]% w/w; CAS RN [redacted]). These options are acceptable as long as you can derive a half-life for the MEK peroxide trimer constituent of the Substance in the test.

To dose the MEK peroxide trimer constituent into the test system, using a solvent or stabilizer or dosing the Substance as such is appropriate.

The results must enable the evaluating MSCA to evaluate the concentration of MEK peroxide trimer in the test systems over time, i.e. not nominal concentrations but analytical concentrations of the main constituent MEK peroxide trimer in the test systems. A maximum test concentration of 100 µg/L is specified in OECD TG 309. However, in paragraph 5 of OECD TG 309, it is noted that higher concentrations (>100 µg/L and sometimes > 1mg/L) may be used if a specific analysis method is not available with a low detection limit to enable measurements of the required accuracy articulated in paragraph 15 of OECD TG309.

You commented that sensitivitiy of analytical methods (using cold, non-radiolabelled, material) may require higher test concentrations than the recommended 100 µg/L. Higher concentrations can be used if analytical methods are not sufficiently sensitive. It is however suggested to use test concentrations as low as technically possible for the results to reflect environmental conditions.

Mass balance and radiolabelled test material versus 'cold' test material

To make a full evaluation of the fate of the MEK peroxide trimer, constituent of the Substance, a mass balance is a prerequisite. The OECD TG 309 suggests that radiolabelled material is most appropriate as test material in the test to achieve a closed mass balance. Alternatively, and as you commented that no contract laboratory was willing to generate radiolabelled peroxide trimer due to its potential explosive properties, non-radiolabelled material can be used provided that a sufficiently sensitive analytical procedure is used to allow for a full mass balance of the MEK peroxide trimer constituent of the Substance and its transformation products.
If no or negligible degradation (less than 30%) is observed in the OECD TG 309, an analytical procedure showing stable parent MEK peroxide trimer concentrations would be sufficient. Carbon dioxide formation from degradation of the MEK peroxide trimer will however be very difficult to quantify as well as abiotic losses and NER formation.

Therefore, sterile controls (as required by OECD TG 309) must be included in the test to determine to what extent decrease in MEK peroxide trimer is due to biotransformation or to potential abiotic losses (e.g. volatilization, formation of non-extractable residues (NER)). By using non-radiolabelled test material, it will not be possible to differentiate whether the observed losses in a sterile control (sterilized surface water including the natural SPM content) are due to loss of the volatile fraction (leakage from test system or sorption to the materials of the test apparatus, e.g. stoppers and tubing) or due to formation of NER. In that case, including also a sterile control containing only purified water, without addition of surface water, will further help the interpretation of the results as the NER formation is minimized, and hence, any potential losses are assumed to be due to loss of the volatile fraction of the test material.

If in a sterile purified water control no loss due to sorption/leakage of the volatile fraction occurs then it can be assumed that negligible losses due to these reasons are occurring in the active test bottles. Therefore, if non-radiolabelled test material is used, sterile purified

water controls must also be included in the test.

Pelagic test (i.e. surface water with a natural content of ~15 mg SPM dw/L)

Information from the surface water simulation test (OECD TG 309) can directly be compared to the P-criterion for the aquatic aerobic compartment in the PBT assessment, if the test is conducted in a way that reflects the environmental conditions of the aquatic aerobic compartment sufficiently well. Although the simulation test guideline allows the possibility to add suspended matter to the water used in the test, the purpose of this specific simulation test is to establish a degradation half life in the aquatic aerobic compartment, and you are requested to perform the test pelagic, i.e. surface water only without addition of suspended solids, and at an environmentally relevant temperature of at most 12°C.

By adding suspended matter or sediment to the test the outcome will not be reflective of the aquatic aerobic compartment, and a combined "system" half-life will be the result. This "system" half-life cannot be directly compared to the P-criterion, and will not allow a proper definitive assessment of the Persistence properties of the registered substance. The amount of suspended particular matter in the pelagic test should be representative of the level of suspended solids in EU surface water. The concentration of suspended solids in the surface water sample used should therefore be approximately 15 mg dw/L[3]. Natural surface water containing between 10 and 20 mg SPM dw/L is considered acceptable.

Furthermore, the presence of suspended matter will further complicate achieving a closed mass balance and interpretation of the test results when using non-radiolabelled ("cold") test material.

Measurement of test material concentration and primary degradation

The concentration of MEK peroxide trimer must be measured at appropriate intervals during the study so that a primary degradation half-life can be determined.

This is required for the following reasons:

- The measurement of the MEK peroxide trimer concentration is important for the comparison between the active test and sterile controls, to estimate the potential contribution of abiotic losses to the decrease in MEK peroxide trimer concentration.
- If a non-radiolabelled test material is used, it will not be possible to accurately determine a mineralisation half-life for MEK peroxide trimer. If CO_2 production measurements are conducted with a non-radiolabelled test material, they would reflect the degradation of the whole substance and not specifically that of MEK peroxide trimer.
- If a radiolabelled test material is used, primary degradation half-life for MEK peroxide trimer is important for the conclusion on the P/vP property, if that degradation half-life based on residual ^{14}C is (i) above the P or vP criterion and (ii) must be determined (in parallel with the determination of a half-life based on residual ^{14}C activity or the evolved $^{14}CO2$).
- Primary degradation half-life of the MEK peroxide trimer may be important for the estimation of the persistence of the transformation products.

Measurement of transformation and/or degradation products

Transformation and/or degradation products detected at ≥10% of the applied

[3] see ECHAs Guidance on information requirements and Chemical Safety Assessment Chapter R.16: Environmental exposure assessment

concentration of the MEK peroxide trimer at any sampling time should be identified unless reasonably justified otherwise. As they may be relevant for PBT/vPvB assessment and, particularly if a non-radiolabelled test material is used, they may also be relevant for obtaining a mass balance of the MEK peroxide trimer. Transformation and/or degradation products of which concentrations are continuously increasing or seem to be stable during the study should also be considered for identification, even if their concentrations do not exceed the limit given above, as this may indicate persistence.

Test temperature

The test must be performed at a temperature of 12°C to represent the average environmental temperature for the EU (as stated in ECHA Guidance R.16, Table R.16-8).

Quantification of NER

It is possible that the Substance in surface water with suspended particular matter (SPM) may form Non Extractable Residues (NER). You have indicated that specifically in OECD TG 307 and 308, testing NER type II formation might interfere with derivation of degradation half-lives. Therefore the most appropriate test is an OECD TG 309 with a maximum content of suspended particulate matter (SPM) of 15 mg/L.

Quantification of non-extractable residues (NER) must be carried out as far as technically feasible. The use of sterile controls, including a sterile purified water control will allow conclusions on the role of NER formation in the interpretation of the test results. 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 Chapter R.11). The Background note on 'Options to address NER in regulatory P assessment', published on the ECHA website, provides some suggestions on the further refinement[4].

Minimisation of losses due to volatisation or sorption

In the tests with other related [redacted] products there were difficulties with keeping the test material in the aqueous system, i.e. biologically available to the bacteria in order to allow them to biodegrade the test material. However, the vapour pressure and aqueous solubility in the registration dossier of the MEK peroxide trimer, constituent of the Substance are not very extreme, giving no reason to expect extreme evaporation of this constituent from the test system. Nevertheless care should be taken to avoid experimental set-up that allows the MEK peroxide trimer to evaporate or sorb to surface materials (e.g. stoppers and tubing).
To address the missing information identified above, the OECD TG 309 will allow to derive a simulated environmental half-life, which is required to conclude whether the main constituent of the Substance – MEK peroxide trimer - fulfils the P- or vP-criterion in the PBT assessment. If simulation testing does not allow for a meaningful derivation of substance half-life (due to technical difficulties, loss of parent substance due to unaccounted processes etc.) you are requested to report the test results in your registration dossier and decide on continuation of the testing (to elucidate B-properties) after consultation of the eMSCA.

[4] https://echa.europa.eu/documents/10162/13632/bg_note_addressing_non-extractable_residues.pdf/e88d4fc6-a125-efb4-8278-d58b31a5d342

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
- access to all information available in the full study report, such as implemented method, raw data collected, interpretations and calculations, consideration of uncertainties, argumentation, and a full mass balance of the MEK peroxide trimer constituent in the Substance and its degradation product.

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 for the main constitituent MEK peroxide trimer of the Substance.

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

The request for the surface water simulation testing is:

- appropriate, because the test is suitable and necessary to obtain information which will allow clarifying whether the main constituent of the Substance (MEK peroxide trimer) has a half-life in surface water which fulfils the P or vP criteria;
- the least onerous measure, because there is no equally suitable alternative methodology available to obtain the information that would clarify the potential hazard.

2.3 Bioaccumulation in fish using aqueous exposure

a) Aim of the study

As detailed in Section 1.1 above, information on bioaccumulation in aquous species of the Substance is required to conclude whether the MEK peroxide trimer, constituent of the Substance, fulfils the B-criterion under REACH. Therefore a study is required that yields a Bioconcentration Factor that can be compared to the B-criterion.

Data on bioaccumulation is requested as a second step in a tiered testing strategy:

- only if the result from Request A.1 shows an environmental half-life exceeding 40 days in the aquatic aerobic compartment (according to the P-criterion in Annex XIII of REACH Annex XIII) or
- only if it is not (technically) feasible to derive a reliable environmental half-life after simulation testing according to OECD TG 309, and where the technical difficulties are properly justified, then this subsequent bioaccumulation study is requested.

Information on bioaccumulation behavior of the petroleum stabilizer is not required, only the main constituent, MEK peroxide trimer is considered a potential ‘B’ substance.

Substance evaluation is the appropriate process to request further data as there is a potential risk based on registration dossier data as well as additional information acquired by the evaluating MSCA (QSAR-modelling and exposure monitoring; sections 1.1 and 1.2). In addition, the study (OECD TG 305) is requested with necessary modifications (monitoring of a specific constituent) to the standard design to ensure that information related to a constituent of concern is provided.
For the purpose of the PBT assessment the information on environmental persistence

should be evaluated first. Therefore data on bioaccumulation is requested as a second step in a tiered testing strategy under the current substance evaluation.

b) Specification of the requested study

Test material and concentration

The test must be performed with the Substance, but you must analyse concentrations specifically for the constituent MEK peroxide trimer. Contrary to the specification for the P-testing, it is considered not appropriate to perform the B-testing with a mixture of MEK- and MPK-peroxide trimer (e.g. in the REACH registered substance 1,2,4,5,7,8-Hexoxonane, 3,6,9-trimethyl-, 3,6,9-tris(Ethyl and Propyl) derivatives (upper limit: 41% w/w; typical concentration: [redacted]% w/w) with CAS [redacted]) to avoid that the presence of MPK-peroxide trimer will influence e.g. the metabolic rate of MEK peroxide, and/or that presence of MPK-peroxide trimer decreases the maxiumum water concentration of MEK-peroxide trimer, which would increase uncertainty in analytical detection.

Using a solvent or stabilizer to dose the constituent into the test system is appropriate as long as these do not influence the bioconcentration behaviour of the MEK peroxide trimer. The results must enable the evaluating MSCA to evaluate the concentration of MEK peroxide trimer in the test systems over time, i.e. not nominal concentrations of the Substance but analytical concentrations of its main constituent, MEK peroxide trimer.

Mass balance and radiolabelled test material

To make a full evaluation of the bioaccumulation of the MEK peroxide trimer, the OECD TG 305 considers the use of radiolabelled test material (i.e. 3,6,9-triethyl-3,6,9-trimethyl-1,2,4,5,7,8-hexaoxonane) optimal. However, with sufficiently sensitive analytical methods the bioconcentration factor in fish may also be determined using non-radiolabelled ('cold') test material.

Aqueous exposure using flow-though system

The solubility of the Substance (13.1 mg/l) and the octanol-water partition coefficient (log Kow = 4.84) in the dossier allows for determination of BCFs using aqueous exposure under flow-through conditions, which yields a BCF value that can be directly compared to the PBT-criteria. Aqueous exposure of fish is feasible for this substance, as the OECD TG305 indicates that the alternative (dietary exposure) test was designed primarily for poorly soluble non-polar organic substances. MEK peroxide trimer is not non-polar, nor poorly soluble according to its water solubility and log Kow values. Based on the aquatic toxicity tests in the dossier, in which a decline of exposure concentrations up to 65% was observed under semi-static conditions, flow-through conditions are required to ensure stable exposure concentrations.

Fish growth and lipid content

Excessive fish growth and lipid increases shall be avoided, since these might confound the results. The results shall be corrected for growth and normalized to 5% lipid content, as specified in the OECD TG 305.

Analytics and radiolabelled material

Experiences from the environmental degradation testing in surface water (Request A.1), including the use of the radiolabelled MEK peroxide trimer and/or the analytical methods developed to characterize non-radiolabelled MEK peroxide trimer in low concentrations must also be applied here.

To address the missing information identified above, the OECD TG 305 will allow to derive a Bioconcentration Factor (BCF), which is required to conclude whether the Substance fulfils the B-criterion in the PBT assessment.

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
- access to all information available in the full study report, such as implemented method, raw data collected, interpretations and calculations, consideration of uncertainties, argumentation and analytical concentrations of the MEK peroxide trimer constituent of the Substance.

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 for the Substance.

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

The request for the bioconcentration testing via aqueous exposure using the Substance is:

- appropriate, because the test is suitable and necessary to obtain information which will allow clarifying whether the Substance is sufficiently bioconcentrating in aqueous species to fulfil the B or vB criteria under REACH;
- the least onerous measure, because there is no equally suitable alternative methodology available to obtain the information that would clarify the potential hazard. You have indicated that you would like to follow an alternative weight of evidence approach by performing *in vitro* S9-rat and fish liver homogenate testing to show metabolism of the Substance will take place. The evaluating MSCA considers that such testing on its own cannot be used to determine a BCF value of the Substance. It is envisaged that the variability in the liver homogenate testing itself will be too high and the interpretation and translation of the *in vitro* metabolic rate constants, obtained with S9-fish liver homogenate testing, to a bioaccumulation potential *in vivo* too uncertain to derive a reliable BCF value.

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

Thomas, K (NIVA), Schlabach M (NILU) *et al*. (2014). Screening programme 2013: New bisphenols, organic peroxides, fluorinated siloxanes, organic UV filters and selected PBT substances. Norsk institutt for vannforskning (NIVA) and Norsk institutt for luftforskning (NILU), published by the Norwegian Environment Agency. ISBN 978-82-577-6431-9. 101 pages.

Thomas, K (NIVA), Schlabach M (NILU) *et al*. (2015). Screening programme 2014: Phosphites, selected PBT substances and non-target screening. Norsk institutt for vannforskning (NIVA) and Norsk institutt for luftforskning (NILU), published by the Norwegian Environment Agency. ISBN 978-82-577-6663-4. 148 pages.

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 the Member State Committee agreed to include the Substance (EC number 429-320-2, CAS RN 24748-23-0) in the Community rolling action plan (CoRAP) to be evaluated in 2019. 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 17 March 2020.

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).

(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.

ECHA referred the draft decision, together with your comments, to the Member State Committee. You did not provide any comments on the proposed amendment(s).

(iii) MSC agreement seeking stage

The Member State Committee reached a unanimous agreement in its MSC-74 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. Adaptations to the test guidelines (e.g. using higher concentrations than suggested) can be made with appropriate justification.

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. In specific cases, when e.g. development of sufficiently sensitive analytical methods hinders the official GLP certification, results generated without GLP certificate could be accepted, provided that suffiencient documentation of the test results is given. Consultation with the evaluating MSCA on any test deviations that would preclude GLP is advised.

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[5].

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, and test results (half-life, BCF) need to be generated specifically for the (single) main constituent of the Substance; the chemical 3,6,9-triethyl-3,6,9-trimethyl-1,2,4,5,7,8-hexaoxonane, also indicated as MethylEthylKetone peroxide trimer or MEK peroxide trimer throughout this Decision.

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. In this case the PBT concern focuses on the main constituent of the Substance, the MethylEthylKetone Peroxide Trimer, or 3,6,9-triethyl-3,6,9-trimethyl-1,2,4,5,7,8-hexaoxonane. Analytical methods should

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

allow to evaluate the actual exposure concentrations maintained during the testing of this constituent in the bioconcentration test, and the concentration of this constituent and its degradation products in the surface water degradation test. Test results (half-life, BCF) should be reported for the main constituent of the Substance, not for the Substance as a whole.

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"[6].

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