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Helsinki, 7 August 2017

Substance name: [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis [tert-butyl] peroxide
EC number: 246-678-3
CAS number: 25155-25-3
Date of Latest submission(s) considered[1]: 17 June 2015
Decision/annotation number: SEV-D-XXXXXXXXXX-XX-XX/F)
Addressees: Registrant(s)[2] of [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis [tert-butyl] peroxide

DECISION ON SUBSTANCE EVALUATION

1. Requested information

Based on Article 46(1) of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), you are requested to submit the following information on the registered substance:

1.1 Simulation testing on ultimate degradation in surface water; test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25. /OECD 309 performed as pelagic test (i.e. surface water with a natural content of ~15 mg SPM dw/L as specified in Appendix 1) at an environmentally relevant temperature of at most 12 °C using the registered substance. The test set-up shall enable to check the mass balance (using radiolabelled substance) and be performed as specified in Appendix I.

If the environmental half-life in the aquatic aerobic compartment determined under information requirement 1.1 exceeds 40 days, you are also requested to submit the following information on the registered substance:

1.2 Bioaccumulation in aquatic species; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD 305, using aqueous exposure. 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. The test shall be conducted in a flow-through system and exposure concentrations shall be monitored during the experiment and expressed as a Time Weighted Average.

If the results from the tests under 1.1 and 1.2 allow to conclude that the substance fulfils the "vPvB" criterion according to Annex XIII of the REACH Regulation, no further information is required under this decision.

If the results from the tests under 1.1 and 1.2 allow to conclude that the substance does not fulfil "vPvB" criterion but fulfils both the 'P' and 'B' criteria according to Annex XIII of

[1] This decision is based on the registration dossier(s) at the end of the 12 month evaluation period.

[2] The terms Registrant(s), dossier(s) or registration(s) are used throughout the decision, irrespective of the number of registrants addressed by the decision.

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the REACH Regulation, you are also requested to submit the following information on the registered substance:

1.3 Long-term toxicity testing on aquatic invertebrates; test method: Daphnia magna reproduction test, EU C.20./OECD 211. The test shall be conducted in a flow-through system and exposure concentrations shall be monitored during the experiment.

If the results from the test under 1.3 does not allow to conclude 'T', you are also requested to submit the following information on the registered substance:

1.4 Long-term toxicity testing on fish; test method: Fish, early-life stage (FELS) toxicity test, OECD 210. The test shall be conducted in a flow-through system and exposure concentrations shall be monitored during the experiment.

You shall provide an update of the registration dossier(s), including robust study summaries and, where relevant, an update of the Chemical Safety Report by the relevant date, as follows:
- if only test 1.1 is required: by **14 May 2019**
- if tests 1.1 and 1.2 are required: by **14 February 2020**
- if tests 1.1, 1.2, and 1.3 are required: by **15 February 2021** or
- if all tests, 1.1, 1.2, 1.3, and 1.4 are required: by **14 February 2022**.

The deadline takes into account the time that you, the Registrant(s), may need to agree on who is to perform any required tests. It has been set to allow for sequential testing or other sequential information gathering or information generation approaches as appropriate.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. Further information, observations and technical guidance as appropriate are provided in Appendix 3. Appendix 4 contains a list of registration numbers for the addressees of this decision. This appendix is confidential and not included in the public version of this decision.

2. Who performs the testing

Based on Article 53 of the REACH Regulation, you are requested to inform ECHA who will carry out the study on behalf of all Registrant(s) within 90 days. Instructions on how to do this are provided in Appendix 3.

3. Appeal

You can appeal this decision to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, shall be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under http://echa.europa.eu/regulations/appeals

Authorised[3] by Leena Ylä-Mononen, Director of Evaluation

[3] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

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Appendix 1: Reasons

Based on the evaluation of all relevant information submitted on [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis [tert-butyl] peroxide and other relevant available information, ECHA concludes that further information is required in order to enable the evaluating Member State Competent Authority (MSCA) to complete the evaluation of whether the substance constitutes a risk to the environment.

The evaluating MSCA will subsequently review the information submitted by you, which shall include the original study reports of the tests requested under 1.1-1.4, and evaluate if further information shall be requested in order to clarify the concern for the potential PBT/vPvB properties of the substance.

The information requested under 1.1, on the persistence in the aquatic compartment, constitutes the first tier in a testing strategy to clarify the concerns for PBT. Hence, you shall review the information submitted under 1.1 as an outcome of tier 1 of the testing strategy, and evaluate if further information as specified in 1.2-1.4 shall be generated in order to clarify the concerns for Bioaccumulation and Toxicity.

Based on the degradation half-life determined in the simulation testing on ultimate degradation in surface water (1.1), a second tier of the testing strategy may be triggered. Based on the bioconcentration factor (BCF) determined in a test on bioaccumulation in fish (1.2), the third tier of the testing strategy may be triggered, if the registered substance meets the criterion for Bioaccumulation according to Annex XIII of the REACH Regulation (BCF >2000). Further information on bioaccumulative properties of the substance and the aquatic long term toxicity may thus be requested sequentially in order to fully evaluate the PBT properties of the registered substance.

The concern for potential PBT status of the substance is increased given a) the detection of the registered substance in recent monitoring studies (see below, Thomas, Schlabach et al. 2015), and b) the wide dispersive emission as evidenced by the presence of a close structural analogue in leachate from a waste site (Thomas, Shlabach et al. 2015).

ENDPOINT 1 Aerobic mineralisation in surface water (information request 1.1)

The Concern(s) Identified

The information in the dossier does not indicate any degradation potential of the substance under environmental, aerobic conditions. Therefore, the concern for a PBT status of the substance is not removed.

Information present in the dossier on the biodegradability of the substance, and used to waive the PBT concern by you, is based upon two test results. Information is given from a screening test (Closed bottle test, OECD 301D) on a close structural analogue (Bis [tert-butyl peroxy isopropyl] benzene, CAS 2212-81-9, EC no 218-664-7). Although the close structural analogue can be considered more biodegradable than the registered substance due to replacement in the structure of two tertiary carbon atoms (2,2-substituted propyl) with two secondary carbon atoms (1,2-substituted propyl), this test

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showed no degradation/mineralization (0%) after 28 days, despite introduction of silica gel to improve bioavailability. A second test in the dossier, performed with the registered substance, is an EPA Subdivision N Pesticide Guideline 162-3 (Anaerobic Aquatic Metabolism) test. This test shows that the registered substance has a half-life of 29 days, at 25°C in this test system. The result of this anaerobic test is used by you as the basis for concluding that the substance is not considered PBT, by claiming that this substance is not persistent (according to the PBT criteria) in the (anaerobic) environment.

As the anaerobic sediment test from the dossier as described above is not a simulation study, it is not possible to compare the half-life from this test directly to the P-criterion for the sediment compartment (substance is considered P if t1/2(sediment) > 120 days). Furthermore the result from this anaerobic test cannot remove the concern for persistence in other (aerobic, aquatic) compartments. You consider that the sediment compartment will be the main compartment of concern since 95% of the test substance was present in the sediment phase at the start of the anaerobic sediment test. However, the test conditions are far from reflecting environmental conditions, i.e. the sediment water ratio is 1:1, the temperature is 25°C. This is a very shallow water layer, which is completely different from the large water columns that are present in the environment. Consequently, results from this laboratory test cannot be used as a measure for the environmental distribution of a substance. Furthermore recent monitoring studies indicate the presence of the registered substance and/or one of the two components of the registered substance (either [1,3- or [1,4-phenylenebis(1-methylethylidene)] bis[tert-butyl] peroxide) in (aerobic) aquatic compartments (Thomas, Schlabach et al., 2015). Earlier monitoring data already indicated the presence of Bis[tert-butyl peroxy isopropyl] benzene (CAS 2212-81-9, EC no 218-664-7), which was used as read across substance for the ready biodegradability study, present in leachate from a waste dump site in Norway, an indication that this substance (which has similar uses as the registered substance) is released from a waste matrix, and not degraded during the residence time in the waste dump [Thomas, Schlabach et al., 2014].

The lack of evidence in the dossier that the registered substance is not exceeding the Persistence-criteria in the PBT assessment, combined with monitoring data showing the presence of this substance in aquatic, aerobic compartments, gives rise to concern that this substance will be able to accumulate in the environment, in food chains, possibly leading to unforeseen long term (ecotoxicological) effects. The potential persistence of the registered substance is confirmed by QSAR calculations. The results from EPIWIN (BioWin 4.10) are 0.0002 (Biowin 2), 1.6027 (Biowin 3) and 0.0069 (Biowin 6), which amply fulfils the screening criteria for potential persistence, as specified in the ECHA's guidance on information requirements and chemical safety assessment; Chapter R.11: PBT/vPvB assessment (November 2014).

Why new information is needed

As indicated, the information on persistence present in the dossier (screening test information on a close structural analogue, anaerobic degration in sediment) is not sufficient to definitely conclude on the persistence of the registered substance in the

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environment, specifically aquatic aerobic compartments. However, the information on the close structural analogue can be considered as a best case for the registered substance and no mineralization was observed in the ready biodegrability test. QSAR estimates confirm the potential persistence. Monitoring data indicate that the substance is detected in aerobic surface waters. Therefore, an estimation of the environmental half-life in that compartment is necessary to evaluate the P-criterion in the PBT assessment.

Considerations on the test method and testing strategy

Information from the simulation test (OECD 309) can directly be compared to the P-criterion for the aquatic aerobic compartment in the PBT assessment, if the test is performed 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 (c.f. ECHAs Guidance on information requirements and Chemical Safety Assessment Chapter R.16: Environmental exposure assessment). Natural surface water containing between 10 and 20 mg SPM dw/L is considered acceptable. It is possible that the registered substance in surface water with suspended particular matter may form non extractable residues (NER). The registrant is requested to justify scientifically that the extraction procedure/solvent chosen is appropriate to completely extract the non-irreversible bound fraction of the substance/its metabolites from the suspended particulate matter (SPM) matrix. Strong extractions, such as soxhlet-extraction with apolar solvents, should be used in order to conclude that the remaining part should be considered as NER. To make a full evaluation of the fate of the registered substance including a mass balance, radiolabelled [1,3(or 1,4)-phenylenebis(1-ethylethylidene)]bis [tert-butyl] peroxide is required as test substance in the test.

Alternative approaches and Proportionality of the request

An OECD 309 simulation test is requested, and not e.g. an OECD 308 Sediment simulation test, as existing (qualitative) information on (anaerobic) sediment degradation is available. The EPA N anaerobic degration test in the dossier is not an environmental simulation study, and also has been performed at an environmentally unrealistic high temperature of 25°C, therefore the half-life determined in this test can not be compared to the P-criterion for the sediment compartment. However, it does give

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a clear indication that the registered substance is susceptible to (anaerobic) breakdown in sediment so this does not need further investigation at this moment. The current concern focuses on the degradation potential in surface water, as monitoring studies have shown the presence of the registered substance in surface water. The OECD 309 test is the most suitable simulation test to adresss this specific concern.

Summary of your Comments and response

You agree to launch the study at the soonest after reception of the final decision. ECHA welcomes the prompt start of the testing. Furthermore, you agree with the proposal(s) for amendment to specify in the Decision the suspended particulate matter (SPM) concentration in the water sample used to perform the OECD TG 309 "pelagic" test.

Conclusion

Based on the substance evaluation and pursuant to Article 46(1) of the REACH Regulation, ECHA concludes that you are required to carry out the following study using a radiolabelled substance subject to this decision: Simulation testing on ultimate degradation in surface water; test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25. /OECD 309, performed as pelagic test (i.e. water only without addition of suspended solids) and at an environmentally relevant temperature of at most 12 °C.

ENDPOINT 2 Bioaccumulation in Fish, aq. exposure (information request 1.2)

The Concern(s) Identified

The value used in the dossier for the log K_{ow} of the registered substance is an estimated value of 7.3, as the experimental procedure only indicates a partition coefficient of >5.5. Both are indicative of the substance potentially meeting the B- or vB-criterion in the PBT assessment (BCF>2000 and >5000 respectively).

In the CSR submitted by you, information from an *in vitro* fish liver S9 metabolism study is included. A BCF value is estimated based on the outcome of an *in vitro* metabolism study in combination with the Arnot-Gobas bioaccumulation model (Arnot and Gobas, 2003). The reported *in vitro* metabolism rate constant is extrapolated to an overall *in vivo* metabolism rate constant on the basis of the publication by Cowan-Ellsberry et al. 2008. Based on the disappearance of the test item, the substance is claimed to be clearly metabolized in the test. The estimated *in vivo* rate for metabolism for the registered substance lowered the estimated BCF that was calculated without any metabolism (45,294) by a factor of at least 85 resulting in BCF values of 209 to 536. This is indicative of the high influence this estimated *in vivo* rate constant has on the estimated BCF.

The Arnot-Gobas model calculates a BCF value based on the assumption that the fish can be considered as a homogeneous compartment, i.e. all the kinetic rate constants k_1 (gill uptake rate constant), k_2 (gill elimination rate constant), k_D (dietary uptake rate constant), k_E (fecal egestion rate constant), k_M (metabolic rate constant), k_G (growth

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rate constant) are defined for the whole fish. The estimated log K_{ow} that is used in the dossier for the registered substance is however significantly higher than the log K_{ow} values of the four substances used for validating the *in vivo* metabolism rate constants (Cowan-Ellsberry et al., 2008). The more hydrophobic a substance is, the slower the internal redistribution kinetics between lipid compartments and blood will become, which will likely reduce the overall metabolism rate. Therefore, ECHA considers the *in vitro* to *in vivo* extrapolation to estimate the overall metabolism rate constant insufficiently validated.

Supporting information for this conclusion comes from the structurally very similar compound, 1,1-bis(tert-butylperoxy)-3,3,5-trimethylcyclohexane (CAS 6731-36-8), which is a shielded peroxide as well (i.e. the peroxide groups are surrounded by tertiary carbon atoms). In the registration on the ECHA dissemination website, a S9 metabolism study is described for this substance similar to the study described above for the registered substance. On basis of that study the estimated BCF without metabolism of 46,097 is lowered to a range 422 to 765, thus also numerically very similar to the registered substance. However, for 1,1-bis(tert-butylperoxy)-3,3,5-trimethylcyclohexane experimental BCF values are available that exceed the vB criterion for bioaccumulation (BCF>5000). In this experimental study, no kinetic data are presented. However, a re-analysis of the reported data by the evaluating MSCA confirmed the high BCF values (kinetic BCF values 7200-7400 L/kg in both low and high concentration for carp with a lipid content of 4.7%. This confirms the high bioaccumulation potential for shielded peroxides despite the assumed hydrolytic reactivity that would lower the BCF.

Some critical remarks can be made to the *in vitro* metabolism study itself ([redacted], 2009). In the study, the concentration of *tert*-butanol, a potential metabolite of the registered substance, is followed as well as the parent substance.

The disappearance of the parent compound from the biologically active S9 incubation is significant, but at the same time highly variable. The coefficient of variation for the three replicates are on average about 50%, but for the 5th time point of the biologically active treatment even exceeds 100%. Thus, the rate of metabolism has wide confidence intervals, but this is not addressed in the registration dossier. Further, on average, the amount disappeared from the heat-treated deactivated test is similar to the biologically active S9 incubation. However, the lowest amounts of parent compound are present at the intermediate time points (3,4,5) for the deactivated incubation, while they are present at the last time points (4,5,6) for the biologically active S9 incubation. The amount of the metabolite in the heat-treated deactivated incubation is about ten times higher than in the biologically active S9 incubation, which can be explained by the fact that the S9 incubation metabolizes *tert*-butanol as well. However, in both treatments there is no significant trend of the concentration of *tert*-butanol in time at all. This is in contradiction with the assumption that *tert*-butanol is formed as a result of metabolic activity during the test. Finally, there is no complete mass balance in this kind of test and without the quantification of all metabolites, the dissipation of the parent compound can be caused by other processes as well. From other tests, such as the reproduction

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test with *Daphnia magna*, it has become clear that it is extremely difficult to maintain aqueous concentrations of the registered substance in a static exposure system.

Why new information is needed

As stated above, both the extrapolation from *in vitro* to the overall *in vivo* metabolism rate constant and the determination of the *in vitro* metabolism rate constant are too uncertain to draw firm conclusion about the bioaccumulation potential of the registered substance and the current conclusion in this regard seems to be flawed (cf. considerations above). Therefore, the substance is potentially bioaccumulative as its log K_{ow} value is amply above the screening criterion for bioaccumulation. Moreover, experimental information from a structurally similar shielded peroxide confirms the potential high bioaccumulation. If the registered substance appears to be persistent as addressed under the first request for information (information request 1.1), the substance is potentially PBT and/or vPvB and more information on the bioaccumulation potential is needed.

Considerations on the test method and testing strategy

The solubility of the substance (0.04 mg/l) allows for determination of BCFs using aqueous exposure under flow-through conditions, which can be directly compared to the PBT-criteria. 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.

Alternative approaches and Proportionality of the request

As stated within Chapter R.11 of ECHA's *Guidance on information requirements and chemical safety assessment* (June 2017), when deciding on the persistence, bioaccumulation or toxicity information required to reach an unequivocal conclusion, vertebrate animal testing must be avoided whenever possible. Therefore, when further information for several properties is required, the assessment should normally clarify the potential for persistence first. When it is clear that the P criterion is fulfilled, a stepwise approach is followed to clarify whether the B criterion is fulfilled.

Therefore, the information requested within the present decision is tiered to first clarify the potential for persistence (request 1.1) before clarifying the potential for bioaccumulation. This approach potentially minimises any subsequent costs, time and experimental studies that may be required to clarify the PBT/vPvB concern.

The OECD 305 test guideline includes a testing option for either aqueous or dietary exposure. As the dietary exposure method does not directly provide a BCF that can be compared to the bioaccumulation criteria, the aqueous exposure shall be used. As stated above, the performance of this test design is regarded as feasible, taking the solubility of the substance into account.

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Summary of your Comments and response

You argue that the solubility of the substance is insufficient to perform aqueous exposure testing. However, according to the OECD 305 test guideline the substance is only close to the water solibility limits indicated for poorly soluble substances. The experience with the semi-static long term daphnia test [[redacted] 2016] also shows that it is possible to prepare stable and reproducible test solutions up to the water solubility of the substance (~0.040 mg/L). However, concentrations in the semi-static long term daphnia test dropped to virually zero after introduction of algae, therefore concentrations should be maintained in a flow through test design. It shall be noted that several examples of aqueous exposure BCF tests (OECD TG 305) on substances with very low water solubilities have been performed successfully. The ambiguity in the interpretation of a (dietary) BMF value, and/or its conversion to a BCF value, in order to compare to the REACH PBT criteria, makes it possible that there remains a need for further, follow-up testing. ECHA maintains the opinion that aqueous exposure testing in the OECD TG 305 is technically feasible, given the experiences reported by the registrant in the semi-static daphnia toxicity test. The low water solubility and adsorptive behaviour of the substance are all arguments to request to perform the BCF-test using a flow-through design.

In your comments on the submitted proposal(s) for amendment, you repeat your opinion that testing via the aqueous exposure route will be technically difficult, but these comments were not related to the proposal(s) for amendment made.

Conclusion

Therefore, based on the substance evaluation and pursuant to Article 46(1) of the REACH Regulation, ECHA concludes that, subject to the condition set in section 1 of the decision, you are required to carry out the following study using a radiolabelled material of the registered substance subject to this decision: Bioaccumulation in aquatic species; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD 305, using the aqueous exposure method. The test shall be conducted in a flow-through system and exposure concentrations shall be monitored during the experiment and endpoints shall be based on time weighted mean measured concentrations.

ENDPOINT 3 Longterm Toxicity testing for Daphnia (information request 1.3)

The Concern(s) Identified

The long term toxicity data in the dossier is a *Daphnia* reproduction test. You updated an earlier *Daphnia* test in the registration dossier [[redacted] 2015] showing shortcomings in constant exposure concentrations by a semi-static limit test (at maximum water solubility) [[redacted] 2016]. This second test, currently in the dossier, shows starting concentrations of the test solutions to be stable and reproducible. However, it is also shown that virtually no aqueous exposure of the daphnids to the substance occurs, because "...the test substance binds instantly to algae cells in significant amounts (almost 100%)". As no aqueous exposure has occurred, no conclusion on the T criterion can be reached from this information.

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Why new information is needed

As concentrations in the current semi-static limit test drop to virtually zero immediately after introducing algae in the system, the test as currently reported [[redacted] 2016] does not allow comparison with the T-criterion in the PBT assesment, as no exposure could be shown in the test (measured exposure concentrations are virtually zero).

Considerations on the test method and testing strategy

As concentrations in the current semi-static limit test drop to virtually zero immediately after introducing algae in the system, it is requested that the test is performed using flow-through system, with monitoring of the concentrations during the test, and showing stable, reproducible exposure concentrations. A flow-through design, including equilibration of the test environment (i.e. conditioning, as described in OECD Guidance Document N°23 – on Aquatic Toxicity Testing of Difficult Substances and Mixtures), most notably of the algae that are introduced in the test system, is required to maintain stable exposure concentrations.

Alternative approaches and Proportionality of the request

Both the static [[redacted] 2015] and the semi-static design of the test [[redacted] 2016] did not lead to acceptable exposure concentrations (either wildly fluctuating, or effectively zero after introduction of algae in the system). Therefore a flow-through design, with equilibration of the test environment (i.e. conditioning, as described in OECD Guidance Document N°23 – on Aquatic Toxicity Testing of Difficult Substances and Mixtures, most notable of the algae that are introduced in the test system), is considered the best approach to guarantee stable exposure concentrations and give a test result that can be compared to the T-criterion for PBT assessment.

Summary of your Comments and response

You propose to accept a limit test with daphnia, where no or negligible aqueous exposure has occurred, and no effects were observed. ECHA considers this test not valid, as no sufficiently high and stable concentrations could be maintained and shown in this test, leading to the conclusion that a flow-through design is required, with sufficient measures, such as equilibrating the test vessels and the algae introduced in the test with test solutions prior to exposure (i.e., conditioning). The flow-through test design is explicitly mentioned in the OECD TG 211 as an option when stable concentrations are difficult to maintain.

In your comments on the proposal(s) for amendment (PfA), you interpret the PfA requesting explanation as to how the flow-through test would reduce/remove reduction of test concentrations (due to the substance binding instantly to algae cells) as indicating that the submitter of the PfA is not in favour of performing the requested long-term toxicity test on aquatic invertebrates. However, the submitter of this PfA also submitted PfAs that favour the standard tiered approach for PBT assessment, i.e. P then B, then T testing, where T testing should follow the order algae, daphnids, fish to ensure no unnecessary vertebrate testing is performed. There is the possibility that long term

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invertebrate testing with actual aquatic exposure (by means of a flow-through test design) leads to the conclusion that the substance can be considered a PBT substance (if the P and the B criterion have already been shown to be met by this substance). In that case, no long-term fish testing would be required, and unnecessary invertebrate testing can be omitted. Therefore this decision reflects the standard tiered approach for PBT assessment, and long-term invertebrate testing (where actual aqueous exposure can be shown) is included before long-term toxicity testing to fish is requested.

Conclusion

Therefore, based on the substance evaluation and pursuant to Article 46(1) of the REACH Regulation, ECHA concludes that, subject to the conditions set in section 1 of the decision, you are required to carry out the following study using the registered substance subject to this decision: Long-term toxicity testing on aquatic invertebrates; test method: *Daphnia magna* reproduction test, EU C.20./OECD 211. The test shall be conducted in a flow-through system with equilibration of the test system and the algae introduced in the test system (i.e. conditioning) and exposure concentrations shall be monitored during the experiment and endpoints shall be based on time weighted mean measured concentrations.

ENDPOINT 4 Longterm Toxicity testing for Fish (information request 1.4)

The Concern(s) Identified

As there is no chronic toxicity data on fish available, and no reliable acute toxicity data for fish, either, no definitive assessment of the T-criterion is yet possible. The concern that this substance might have PBT properties requires evaluation of the T-properties of this substance.

Why new information is needed

Long-term fish toxicity data is not present in the dossier. Acute toxicity data for fish is only available from read across to a close structural analogue, and is reported only in nominal concentrations (with the nominal concentration several orders of magnitude above the aqueous solubility). The acute toxicity data is therefore unsuitable to determine the most sensitive species. Furthermore, the long-term *Daphnia magna* reproduction test in the dossier is unreliable (as indicated by the registrant) due to difficulties with getting stable, reproducible, exposure concentrations. Nevertheless the study has been reported and is used to determine PNECs and RCRs in the CSR. The registrant does indicate in the dossier that currently studies are undertaken to improve on the generation of test solution in order to solve the problem with the unstable exposure conditions.

Considerations on the test method and testing strategy

The results of the long-term toxicity testing are to be used for evaluation of the T-criterion in the PBT assessment. Therefore, long-term aquatic toxicity studies where exposure concentrations shall be kept as constant as possible are required. A flow-

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through design is therefore considered necessary, as the semi-static approach to long-term toxicity testing with daphnia currently presented in the dossier shows that this semi-static design leads to very low or negligible aqueous exposure.

Alternative approaches and Proportionality of the request

The updated limit test (at water solubility, ~40 µg/L*) Daphnia magna* reproduction study did not show any effects, but could also not show that actual (aquatic) exposure has taken place during the test, making the derivation of a PNEC and the calculation of risk to the aquatic environment impossible. If a more accurate performance of the long-term *Daphnia magna* test also does not meet the T criterion, further long term toxicity testing is required. The long-term fish toxicity test is the only test which will allow taking into account a third trophic level in the derivation of the PNEC and for the PBT assessment. As no valid fish toxicity information is available, it cannot be excluded that fish will be the most sensitive species.

Summary of your Comments and response

You propose to perform the long term fish toxicity testing immediately (in parallel with the ultimate mineralization testing, information request 1.1), and use a semi-static design comparable to the current updated long term daphnia test in the registration dossier. This (updated) long term daphnia test is not considered valid by ECHA, therefore *first* the long term toxicity to daphnia will have to be evaluated properly, using flow-through testing, and proving aqueous exposure has taken place by monitoring concentrations throughout the test (information request 1.3). In the tiered testing for PBT properties described in the REACH guidance, toxicity testing is seen as the last step, after BCF testing has taken place. If after evaluating the information requests 1.1, 1.2 and 1.3, the substance can already be considered PBT or vP and vB, or if the substance is considered 'not P' and/or 'not B', no further toxicity testing needs to be performed. The initial order of the tiered testing strategy as proposed in the draft decision dated 26 April 2016, was therefore changed to reflect the order as given in the REACH guidance document R11, i.e. P, then B, then T.

In your comments on the proposal(s) for amendment to further explain the concern(s) that this information requirement will clarify and consideration of a tiered approach, you propose to start testing long term toxicity to fish immediately, with the argument that this is the only option left to generate information to derive PNECs for the aquatic compartment and allow for a quantitative risk assessment.

Furthermore, you consider that the flow-through system is not appropriate for the registered substance due to its water solubility and being very adsorptive, preventing substance concentrations to be satisfactorily maintained. This statement contradicts your previous comments with regard to information request 1.3 (long term toxicity testing for Daphnia) where you stated: "... *These investigations have indicated that a slowly stirred stock solution of 10 mg/L stirred for an extended period generates a relatively stable and reproducible concentration of test substance at its solubility limit in test medium. ..... The analytical data demonstrated that the parent material was present in all of the*

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measured fresh test solution throughout the test at stable and reproducible concentrations.". If you were able to maintain stable and reproducible test concentrations at the start of this semi-static test ECHA considers it also possible to have a flow through test design for the OECD 211 test that creates stable and reproducible concentrations.

ECHA therefore thinks that a flow-through test design is feasible. Furthermore the use of a flow-through design is deemed necessary, given the experience with the semi-static test design in the daphnia test.

In this decision, the only concern identified for this substance is the PBT/vPvB concern, therefore the information request follows the standard tiered approach for PBT assessment. Furthermore, there is the possibility that a new long term toxicity test with invertebrates that shows actual aquatic exposure already allows to conclude on the PBT concern. In that case long term toxicity testing to fish would be unnecessary and toxicity testing on vertebrates can be avoided.

Conclusion

Therefore, based on the substance evaluation and pursuant to Article 46(1) of the REACH Regulation, ECHA concludes that , subject to the conditions set in section 1 of the decision, you are required to carry out the following study using the registered substance subject to this decision: Long-term toxicity testing on fish; test method: Fish, early-life stage (FELS) toxicity test, OECD 211. The test shall be conducted in a flow-through system and exposure concentrations shall be monitored during the experiment and endpoints shall be based on time weighted mean measured concentrations.

Time needed to perform requested tests and to update the dossier

In your comments, you consider that a timeline of 40 months is necessary to provide a simulation biodegradation test, fish bioaccumulation test, and long-term aquatic toxicity test, on the basis of the test complexity and time required to update the dossier and chemical safety assessment.

ECHA notes that the current deadline of 42 months to submit the requested simulation biodegradation test (1.1), fish bioaccumulation test (1.2), and a long-term toxicity test on aquatic invertebrates (1.3) is above the 40 months that you propose. Furthermore the experience gained in the test design, analytical program and sourcing of radiolabelled test substance when initially performing the requested simulation biodegradation test (1.1) may be applied to the subsequent fish bioaccumulation test and thus may result in additional time gains. ECHA therefore considers that the deadline set is reasonable for performing the tests, administration and submission of the information to ECHA.

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Appendix 2: Procedural history

On the basis of an opinion of the ECHA Member State Committee and due to initial grounds for concern relating to PBT/vPvB, [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis [tert-butyl] peroxide CAS No 25155-25-3 (EC No 246-678-3) was included in the Community rolling action plan (CoRAP) for substance evaluation to be evaluated in 2015. The updated CoRAP was published on the ECHA website on 17 March 2015. The Competent Authority of the Netherlands (hereafter called the evaluating MSCA) was appointed to carry out the evaluation.

Pursuant to Article 45(4) of the REACH Regulation the evaluating MSCA carried out the evaluation of the above substance based on the information in your registration(s) and other relevant and available information.

The evaluating MSCA considered that further information was required to clarify the PBT concern. Therefore, it prepared a draft decision pursuant to Article 46(1) of the REACH Regulation to request further information. It submitted the draft decision to ECHA on 16 March 2016.

The decision making followed the procedure of Articles 50 and 52 of the REACH Regulation.

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

Registrant(s)' commenting phase

ECHA received comments from you and forwarded them to the evaluating MSCA without delay.

The evaluating MSCA considered the comments received from you. These comments lead the evaluating MSCA to modify its requirements. Some clarifications were also added in Reasons (Appendix 1).

Proposals for amendment by other MSCAs and ECHA and referral to 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 from one Member State and ECHA.

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 proposal(s) for amendment were taken into account by the Member State Committee and are reflected in the Reasons (Appendix 1). The Member State Committee did not take into account any comments on the draft decision as they were not related to the proposal(s) for amendment made and are therefore considered outside the scope of

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Article 52(2) and Article 51(5).

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-54 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

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Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided by you in the registration(s) is in compliance with the REACH requirements. The decision neither prevents ECHA from initiating compliance checks on your dossier(s) at a later stage, nor does it prevent a subsequent decision under the current substance evaluation or a new substance evaluation process once the present substance evaluation has been completed.

2. Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the required experimental studies, the sample of the substance to be used shall have a composition that is within the specifications of the substance composition that are given by all Registrant(s). It is the responsibility of all the Registrant(s) to agree on the tested material to be subjected to the test(s) subject to this decision and to document the necessary information on composition of the test material. The substance identity information of the registered substance and of the sample tested must enable the evaluating MSCA and ECHA to confirm the relevance of the testing for the substance subject to substance evaluation.

4. In relation to the experimental studies the legal text foresees the sharing of information and costs between Registrant(s) (Article 53 of the REACH Regulation). You are therefore required to make every effort to reach an agreement regarding each experimental study for every endpoint as to who is to carry out the study on behalf of the other Registrant(s) and to inform ECHA accordingly within 90 days from the date of this decision under Article 53(1) of the REACH Regulation. This information shall be submitted to ECHA using the following form stating the decision number above at:
https://comments.echa.europa.eu/comments_cms/SEDraftDecisionComments.aspx

   Further advice can be found at
http://echa.europa.eu/regulations/reach/registration/data-sharing . If ECHA is not informed of such agreement within 90 days, it will designate one of the Registrants to perform the stud(y/ies) on behalf of all of them.