EUROPEAN CHEMICALS AGENCY

Helsinki, 5 December 2017

Addressee: [redacted]

Decision number: CCH-D-2114381462-49-01/F
Substance name: Ethylenebis(oxyethylene) bis[3-(5-tert-butyl-4-hydroxy-m-tolyl)propionate]
EC number: 253-039-2
CAS number: 36443-68-2
Registration number: [redacted]
Submission number: [redacted]
Submission date: 25/04/2017
Registered tonnage band: 100-1000

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: Alga, growth inhibition test, EU C.3./OECD TG 201) with the registered substance;**

2. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with the registered substance;**

3. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with the registered substance;**

4. **PBT and vPvB assessment of relevant constituents and degradation products (Article 14 (3)(d) in conjunction with Annex I, Section 4 and Annex XIII);**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI to the REACH Regulation. To ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by **12 December 2018**. You also have to update the chemical safety report, where relevant.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to 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[1] by Kevin Pollard, Head of Unit, Evaluation E1

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

Appendix 1: Reasons

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

1. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided a study record for the key study (reference title: "*Report on the Growth inhibition test of the test item to Green Algae (Scenedesmus subspicatus)*"). However, this study does not provide the information required by Annex VII, Section 9.1.2., because it is not reliable as explained in the following.

ECHA observes that in the study summary provided in the registration dossier you note a number of deviations to the standard OECD TG 201 Alga, growth inhibition test. More specifically you mention that "*initial biomass, growth rate and yield not reported, coefficient of variation was not calculated [...] test concentration was not verified; use of emulisifier, testing of doses exceeding limit of water solubility; growth rate and yield, standard deviation not reported; pH increased >1.5*". ECHA considers that validity of the study cannot be confirmed as it cannot be verified whether or not performance criteria listed in the paragraph 11 of the OECD TG 201 were met. Therefore, ECHA considers that the results of the key study reported in the registration dossier are not adequate for the purpose of classification/labelling and risk assessment.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Algae growth inhibition test, EU C.3./OECD TG 201).

Notes for your consideration

Due to the low solubility of the substance in water and potential of the substance to adsorb to solid matter you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity tests and for calculation and expression of the result of the tests.

2. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided a study record for the key study (reference title: "[redacted]") which was performed with the analogue substance *thiodiethylene bis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate] / sulfanediyldiethane-2,1-diyl bis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propanoate]* (CAS number 41484-35-9, EC number 255-392-8). ECHA understands that for the long-term toxicity testing on aquatic invertebrates endpoint you have sought to adapt the information requirements listed above by applying a read-across approach in accordance with Annex XI, Section 1.5. According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (read-across approach). ECHA considers that the generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a toxicological or ecotoxicological property is reliable and should be based on recognition of the structural similarities and differences between the source and registered substances. This hypothesis explains why the differences in the chemical structures should not influence the toxicological/ecotoxicological properties or should do so in a regular pattern. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures. There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case.

Due to the different nature of each endpoint and consequent difference in scientific considerations (e.g. key parameters, biological targets), a read-across must be specific to the endpoint or property under consideration.

Key physicochemical properties may determine the fate of a compound, its partitioning into a specific phase or compartment and largely influence the availability of compounds to organisms, e.g. in bioaccumulation and toxicity tests. Similarly, biotic and abiotic degradation may alter the fate and bioavailability of compounds as well as be themselves hazardous, bioaccumulative and/or persistent. Thus, physicochemical and degradation properties influence the human health and environmental properties of a substance and should be considered in read-across assessments. However, the information on physicochemical and degradation properties is only a part of the read-across hypothesis, and it is necessary to provide additional justification which is specific to the endpoint or property under consideration.

The ECHA Read-across assessment framework foresees that there are two options which may form the basis of the read-across hypothesis- (1) (Bio)transformation to common compound(s)- the read-across hypothesis is that different substances give rise to (the same) common compounds to which the organism is exposed and (2) Different compounds have the same type of effect(s)- the read-across hypothesis is that the organism is exposed to different compounds which have similar (eco)toxicological and fate properties as a result of structural similarity (and not as a result of exposure to common compounds).

Finally, Annex XI, Section 1.5. lists several additional requirements, which deal with the quality of the studies which are to be read-across.

You consider to achieve compliance with the REACH information requirements for the registered substance *Ethylenebis(oxyethylene) bis[3-(5-tert-butyl-4-hydroxy-m-tolyl)propionate]* using data of structurally similar substance *thiodiethylene bis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate] / sulfanediyldiethane-2,1-diyl bis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propanoate]* (CAS number 41484-35-9, EC number 255-392-8) (hereafter the 'source substance').

You have provided a category justification document ("[redacted]") as a separate attachment in the section 6.1.4 of the registration dossier. According to the information reported in the category justification document, the substance subject to this decision is a member of the "[redacted]" category. You have identified the members of the category (4): N,N'-hexane-1,6-diylbis[3-(3,5-ditert-butyl-4-hydroxyphenylpropionamide] (EC number 245-442-7), 2',3-bis[[3-[3,5-di-tert-butyl-4-hydroxyphenyl]propionyl]]propionohydrazide (EC number 251-156-3), ethylenebis(oxyethylene) bis[3-(5-tert-butyl-4-hydroxy-mtolyl)propionate] (EC number 253-039-2) and thiodiethylene bis[3-(3,5-di-tertbutyl-4-hydroxyphenyl)propionate] (EC number 255-392-8).

You use the following arguments to support the prediction of properties of the registered substance from data for source substances within the group:

"*The hypothesis is that none of the category members have toxic effects – neither acute nor chronic – on aquatic organisms due to limited bioavailability resulting in the absence of the chemicals at the biological targets. Due to the high structural similarity, the substances are expected to have qualitatively similar properties. This assumption is reflected by the available reliable toxicity studies that did not show any toxic effects towards the test organisms.*

Besides these aspects, the aquatic compartments are not the relevant compartments for these substances due to their similar distribution and partitioning behavior. The very low water solubility and the high logKow values are clear proof of very low concentrations in the water compartments and thus, negligible bioavailability resulting in the absence of toxic effects. The compounds are expected to bind to organic carbon and therefore, soil and/or sediment are assumed to be the relevant compartments." [...] "*The structural differences between the category members neither change the principal physical-chemical properties nor the environmental fate and ecotoxicity results (not readily biodegradable, not bioaccumulative due to molecular size and metabolic transformation, no toxicity due to reduced bioavailability and absence at the biological targets).*"

As an integral part of this prediction, you propose that the source and registered substance(s) have similar properties for the above-mentioned information requirement. ECHA considers that this information is your read-across hypothesis.

ECHA has assessed your grouping approach against the requirements of Annex XI, section 1.5. and observes the following deficiencies.

ECHA notes that while you list the 4 category members, you do not define unambiguously the applicability domain of the proposed category. You have provided a "*qualititative analysis of the structural similarity covering functional chemical groups*" and indicated that "*With the exception of CAS 36443-68-2 the category members share two 3-(3,5-ditert-butyl-4-hydroxy-phenyl)propanoic acid groups or two 3-(3,5-ditert-butyl-4-hydroxy-phenyl)propanamide groups connected with a carbon chain which can contain oxygen and/or sulphur. CAS 36443-68-2 exhibits a methyl group at position 5 of the phenol ring instead of a tert-butyl group*". Information on applicability domain is necessary to outline possible differences among the category members and constitutes a set of inclusion and exclusion rules establishing the molecular structure(s) that a substance must have to be part of the category and describing the accepted structural differences within the category. You have not defined these inclusion and exclusion criteria, such as e.g. substituents in the phenol ring, length range and functional groups allowed in the alkly chain. According to ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6, such criteria should be described in order to identify the range of values within which reliable estimations can be made for the members of the category and to define the borders of the category. ECHA considers that the general statement included in the category justification document does not characterise boundaries of the category.

Given that the category definition is not clear, ECHA is unable to verify that the substances in the category can be used so that human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach). Nevertheless, the determination that the grouping is insufficiently defined, and thereby fails to provide a basis for prediction in accordance with Annex XI, 1.5. does not affect the possibility for you to invoke a read-across approach in order to predict environmental effects of these substances individually on the basis of a one-to-one analogue approach.

ECHA observes, as noted also by yourself, that the registered substance has a methyl group at position 5 of the phenol ring instead of a tert-butyl group for other category members, including the source substance. Furthermore, the registered substance has a carbon chain containing only oxygen atoms while other category members have a carbon chain containing nitrogen or sulphur atoms. Thus, there are structural diferences between the registered substance and the source substance.

Moreover, ECHA observes that out of four category members reported in the read-across justification document toxicity data for aquatic invertebrates is available only for the source substance (ECHA considers long-term toxicity study for the source substance with aquatic invertebrates reported in the registration dossier to be reliable). ECHA notes that the results of the algae toxicity key study reported in the registration dossier are not adequate for the purpose of classification/labelling and risk assessment, and that the short-term toxicity tests with aquatic organisms might not be sufficient for the substance as the lack of toxicity at the short-term test cannot exclude long-term toxicity. Thus, there are no adequate data for comparison of toxicity to aquatic organisms of the target substance with other category members.

Furthermore, on the basis of the data matrix provided in the read-across justification document, the registered substance might have higher water solubility and lower octanol-water partitioning coefficient than other category members, incuding the source substance. Thus, ECHA considers that the bioavailability of the registered substance to the aquatic organisms might be higher than of other category members (*e.g.* short-term fish toxicity study with the registered substance indicates some toxicity of the substance, above water solubility limit, to fish). ECHA concludes that the presented evidence in the data matrix does not support a similar or regular pattern of toxicity as a result of structural similarity. Therefore, it cannot be verified that the proposed group/analogue substance can be used to predict properties of the registered substance. The provided explanation is not considered as valid to establish a scientific credible link between the structural similarity and the prediction.

Finally, ECHA observes that there is no environmental exposure assessment reported in the CSR. ECHA considers that based on the uses of the substance identified in the registration dossier environmental exposure cannot be ruled out (e.g. the release of unreacted substance from industrial sites or from articles). Thus, ECHA concludes that the lack of exposure of aquatic environment is not sufficiently justified by you.

Thus, ECHA does not consider the read-across justification to be a reliable basis to predict long-term toxicity testing on aquatic invertebrates for the registered substance for the reasons set out above. The adaptation does not comply with the general rules of adaptation as set out in Annex XI, 1.5. Therefore, ECHA rejects your adaptation in the technical dossier that is based on Annex XI, 1.5.

Furthermore, ECHA considers that substances poorly soluble in water require longer time to be significantly taken up by the test organisms and so steady state conditions are likely not to be reached within the duration of a short-term toxicity test. For this reason, short-term tests may not give a true measure of toxicity for such substances and toxicity may actually not even occur at the water solubility limit of the substance if the test duration is too short. Still, long-term toxicity cannot be excluded and needs to be investigated already at the tonnage band currently applicable for the substance subject to the present decision. ECHA notes that based on information provided in the registration dossier the substance is poorly water soluble (WS<1mg/l). Thus, ECHA considers that short-term toxicity test with aquatic invertebrates might not be sufficient for the substance as the lack of toxicity at the short-term test cannot exclude long-term toxicity.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) *Daphnia magna* reproduction test (test method EU C.20. / OECD TG 211) is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Daphnia magna reproduction test (test method: EU C.20./OECD TG 211).

3. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. Adequate information on Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.), or Fish, short-term toxicity test on embryo and sac-fry stages (Annex IX, 9.1.6.2.), or Fish, juvenile growth test (Annex IX, 9.1.6.3.) needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.6., column 2. You provided the following justification for the adaptation: "*In Annex IX of Regulation (EC) No 1907/2006, it is laid down that a study on long-term toxicity to fish shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on fish. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or is assessed to be a PBT or vPvB. The hazard assessment of the substance reveals neither a need to classify the substance as dangerous to the environment, nor is it a PBT or vPvB substance, nor are there any further indications that the substance may be hazardous to the environment. Therefore, and for reasons of animal welfare, a long-term toxicity study in fish is not provided.*"

According to the ECHA's Guidance on Information Requirements and chemical Safety assessment, Chapter R.7b (version 4.0, June 2017) substances with water solubility below 1 mg/L or below the detection limit of the analytical method of the test substance are considered to be poorly water soluble. Based on information provided in the registration dossier ECHA considers substance to be poorly soluble in water (water solubility of the substance is 0.104 mg/l at 23 °C and pH 7).

ECHA considers that substances poorly soluble in water require longer time to be significantly taken up by the test organisms and so steady state conditions are likely not to be reached within the duration of a short-term toxicity test. For this reason, short-term tests may not give a true measure of toxicity for such substances and toxicity may actually not even occur at the water solubility limit of the substance if the test duration is too short. Still, long-term toxicity cannot be excluded and needs to be investigated already at the tonnage band currently applicable for the substance subject to the present decision.

ECHA acknowledges that there is short-term toxicity study with fish reported in the dossier where no toxicity was observed at the water solubility limit of the substance. However, ECHA considers that short-term toxicity test with fish is not sufficient for the substance as the lack of toxicity in the short-term test cannot exclude long-term toxicity.

Moreover, ECHA notes that the information on toxicity to fish is necessary for the proper Chemical Safety Assessment of the substance. As noted in the Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7b (ECHA, version 4.0, June 2017) standard information on aquatic toxicity (on aquatic invertebrates, fish and aquatic plants) is necessary to enable the environmental hazard assessment, i.e. for use in classification and labelling and derivation of the PNECwater (Predicted No Effect Concentration for water), and for determination of the toxicity (T) criterion in the PBT assessment.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) fish early-life stage (FELS) toxicity test (test method OECD TG 210), fish short-term toxicity test on embryo and sac-fry stages (test method EU C.15. / OECD TG 212) and fish juvenile growth test (test method EU C.14. / OECD TG 215) are the preferred tests to cover the standard information requirement of Annex IX, Section 9.1.6.

However, the FELS toxicity test according to OECD TG 210 is more sensitive than the fish, short-term toxicity test on embryo and sac-fry stages (test method EU C.15 / OECD TG 212), or the fish, juvenile growth test (test method EU C.14. / OECD TG 215), as it covers several life stages of the fish from the newly fertilized egg, through hatch to early stages of growth (see ECHA *Guidance on information requirements and chemical safety assessment, Chapter R7b* (version 4.0, June 2017), *Figure R.7.8-4).*

Moreover, the FELS toxicity test is preferable for examining the potential toxic effects of substances which are expected to cause effects over a longer exposure period, or which require a longer exposure period of time to reach steady state (ECHA *Guidance Chapter R7b,* version 4.0, June 2017).

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

4. PBT and vPvB assessment of relevant constituents and degradation products (Article 14 (3)(d) in conjunction with Annex I, Section 4 and Annex XIII)

According to Article 14 (3) of the REACH Regulation a chemical safety assessment of a substance shall include persistent, bioaccumulative and toxic (PBT) and very persistent and very bioaccumulative (vPvB) assessment. Annex I, Section 4 of the REACH Regulation notes that the objective of the PBT and vPvB assessment shall be to determine if the substance fulfils the criteria given in Annex XIII and if so, to characterise the potential emissions of the substance. Pursuant to Annex XIII of the REACH Regulation the identification of the PBT and vPvB substances shall also take account of the PBT/vPvB-properties of relevant constituents of a substance and relevant transformation and/or degradation products.

ECHA's Guidance, *Chapter R.11: PBT/vPvB asessment* (version 3.0, June 2017), explains that the term "constituent" refers to the main constituents, impurities and additives of substances of well-defined composition and constituents of UVCB substances. Furthermore, in this Guidance document it is noted that the registrant should make efforts for carrying out a PBT/vPvB assessment for all constituents, impurities and additives present in concentrations above 0.1% (w/w). Similar arguments apply to relevant transformation/degradation products. The PBT/vPvB assessment should normally be carried out for each relevant transformation or degradation product.

ECHA observes that in the composition of the substance reported in the registration dossier there is a number of impurities with typical concentration above 0.1 %(w/w). Furthermore, ECHA notes that a list of predicted degradation products is reported in one of the files attached in the registration dossier in IUCLID section 5.2.1.

ECHA notes that you have concluded that the substance is neither PBT nor vPvB. However, it is not clear whether or not this conclusion is valid only for the main constituent of the substance, i.e. [redacted] (EC number 253-039-2), or adresses relevant impurities also. Furthermore, ECHA notes there are no results of PBT/vPvB assessment for the relevant degradation products reported in the registration dossier. Thus, ECHA considers that results of PBT/vPvB assessment of relevant constituents and degradation products is missing in the registration dossier and CSR, Section 8.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation you are requested to provide PBT and vPvB assessment of relevant constituents and degradation products.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 12 May 2017.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

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

ECHA did not receive any comments by the end of the commenting period.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

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

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

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.