EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114336562-52-01/F Helsinki, 14 July 2016

DECISION ON TESTING PROPOSAL(S) SET OUT IN A REGISTRATION PURSUANT TO ARTICLE 40(3) OF REGULATION (EC) NO 1907/2006

For bis(4-tert-butylcyclohexyl) peroxydicarbonate, CAS No 15520-11-3 (EC No 239-557-1), registration number: [redacted]

Addressee: [redacted]

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

I. Procedure

Pursuant to Article 40(1) of the REACH Regulation, ECHA has examined the following testing proposals submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12(1)(d) thereof for bis(4-tert-butylcyclohexyl) peroxydicarbonate, CAS No 15520-11-3 (EC No 239-557-1), submitted by [redacted] (Registrant).

- Developmental toxicity / teratogenicity study (OECD 414)
- 90-day oral toxicity study (OECD 408)
- Biodegradation in water and sediment (OECD 308)

This decision is based on the registration dossier as submitted with submission number [redacted], for the tonnage band of 100 to 1000 tonnes per year. This decision does not take into account any updates after 27 March 2015.

This decision does not imply that the information provided by the Registrant in his registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

ECHA received the registration dossier containing the above-mentioned testing proposals for further examination pursuant to Article 40(1) on 27 March 2013.

ECHA held a third party consultation for the testing proposals from 15 July 2014 until 29 August 2014. ECHA did not receive information from third parties.

On 13 November 2014 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

On 19 December 2014 ECHA received comments from the Registrant on the draft decision.

The ECHA Secretariat considered the Registrant's comments. The statement of reasons (Section III) was changed accordingly.

On 3 March 2016, ECHA notified the Competent Authorities of the Member States of its draft decision and invited them pursuant to Article 51(1) of the REACH Regulation to submit

proposals for amendment of the draft decision within 30 days of the receipt of the notification.

Subsequently, proposal(s) for amendment to the draft decision were submitted.

On 8 April 2016, ECHA notified the Registrant of the proposal(s) for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on the proposals for amendment within 30 days of the receipt of the notification.

The ECHA Secretariat reviewed the proposal(s) for amendment received and amended the draft decision.

On 18 April 2016 ECHA referred the draft decision to the Member State Committee.

By 10 May 2016, the Registrant did not provide comments on the proposal(s) for amendment. However, the Registrant provided comments on the draft decision. The Member State Committee did not take into account the Registrant's 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 Article 51(5).

A unanimous agreement of the Member State Committee on the draft decision was reached on 23 May 2016 in a written procedure launched on 13 May 2016.

ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Testing required

A. Tests required pursuant to Article 40(3)

The Registrant shall carry out the following proposed tests pursuant to Article 40(3)(a) and 13(4) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31/OECD 414) in rats or rabbits, oral route.

The Registrant shall carry out the following modified test pursuant to Article 40(3)(b) and 13(4) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

2. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26/OECD 408) in rats modified to include urinalysis and a full histopathological examination which is to include immunohistochemical investigation of renal pathology to determine if the pathology is mediated by alpha-2u globulin nephropathy;

The Registrant shall carry out the following (additional) tests pursuant to Article 40(3)(c) and (a) and Article 13(4) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

3. Biotic degradation testing

a) Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: Aerobic mineralisation in surface water - simulation biodegradation test, EU C.25/OECD 309) at a temperature of 12 °C;

b) Soil simulation testing (Annex IX, Section 9.2.1.3.; test method: Aerobic and anaerobic transformation in soil, EU C.23/OECD 307) at a temperature of 12 °C;

c) Sediment simulation testing (Annex IX, Section 9.2.1.4.; test method: Aerobic and anaerobic transformation in aquatic sediment systems, EU C.24/OECD 308) at a temperature of 12 °C.

d) Including the identification of the degradation products (Annex IX, Section 9.2.3.) by means of one of the above test methods.

Note for consideration by the Registrant:

The Registrant 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 of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring to and conforming with the appropriate rules in the respective Annex, and an adequate and reliable documentation.

Failure to comply with the requests in this decision, or to fulfil otherwise the information requirements with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

B. Deadline for submitting the required information

Pursuant to Articles 40(4) and 22(2) of the REACH Regulation, the Registrant shall submit to ECHA by **21 January 2019** an update of the registration dossier containing the information required by this decision, including, where relevant, an update of the Chemical Safety Report. The timeline has been set to allow for sequential testing as appropriate.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposals submitted by the Registrant for the registered substance.

A. Tests required pursuant to Article 40(3)

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

A pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

The Registrant has submitted a testing proposal for a pre-natal developmental toxicity study according to EU B.31/OECD 414.

ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

The Registrant did not specify the species to be used for testing. He did not specify the route for testing. According to the test method EU B.31/OECD 414, the rat is the preferred rodent species, the rabbit the preferred non-rodent species and the test substance is usually administered orally. ECHA considers these default parameters appropriate and testing should be performed by the oral route with the rat or the rabbit as a first species to be used.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is requested to carry out the proposed study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in rats or rabbits, oral route (test method: EU B.31/OECD 414).

2. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(b) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test under modified conditions.

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

The Registrant has submitted a testing proposal for a sub-chronic toxicity study (90 day) via the oral route (EU B.26/OECD 408).

ECHA considers that the proposed study via the oral is appropriate to fulfil the information requirement of Annex IX, Section 8.6.2. of the REACH Regulation.

The registered substance is a solid. Based on the particle size distribution, possibility of exposure to particles of inhalable size is low. Consequently, no inhalation exposure to the substance is anticipated and the inhalation route is not an appropriate route for testing. Therefore, ECHA considers that testing by the oral route is most appropriate.

The Registrant did not specify the species to be used for testing. According to the test method EU B.26/OECD 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

In the oral 28-day study, "Hyaline droplets in corticotubular cells of the male kidneys were considered to represent a2-microglobulin, a male rat-specific protein". The dose levels at which these effects were seen were not indicated. The fact that these effects were only observed in male rats indicates that the registered substance may induce alpha-2u-globin-mediated nephropathy. Since humans do not excrete alpha-2u-globin, this mode of action is not relevant to humans. For this reason, ECHA decided to modify the Registrant's testing proposal by including urinalysis (which is optional in paragraph 30 of OECD 408, and the relevant part of Section 1.5.2.2. of EU Method B.26) to investigate kidney function, and a full histopathological examination (paragraph 36 of OECD 408, Section 1.5.2.4. of EU

Method B.26), which is to include immunohistochemical investigation of renal pathology to determine if the pathology is indeed mediated by alpha-2u globulin.

b) Outcome

Therefore, pursuant to Article 40(3)(b) of the REACH Regulation, the Registrant is requested to carry out the modified study with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD 408) modified to include urinalysis and a full histopathological examination which is to include immunohistochemical investigation of renal pathology to determine if the pathology is mediated by alpha-2u globulin nephropathy.

3. Biotic degradation testing (Annex IX, Section 9.2.1.)

a) Examination of the testing proposal
Pursuant to Article 40(3)(c) and (a) of the REACH Regulation, ECHA may require a registrant to carry out a proposed test, and require the registrant to carry out one or more additional tests in case of non-compliance of the testing proposal with Annexes IX, X or XI.

According to column 1 of Section 9.2. (9.2.1.2., 9.2.1.3. and 9.2.1.4.) of Annex IX of the REACH Regulation, simulation testing on ultimate degradation in surface water is a standard information requirement and simulation testing in soil and sediment are standard information requirements for substances with high potential for adsorption to soil or sediment respectively. The information on these endpoints is not available for the registered substance, but needs to be present in the technical dossier to meet the information requirements if the chemical safety assessment (CSA) according to Annex I of the REACH Regulation indicates the need to investigate further the degradation of the substance and its degradation products.

The Registrant has submitted a testing proposal for an Aerobic and Anaerobic Transformation in Aquatic Sediment Systems study (EU C.24/OECD 308). However, in the Chemical Safety Report the testing proposal is under the heading "Simulation testing on ultimate degradation in surface water", which is an Annex IX, Sections 9.2.1.2. requirement. ECHA considers that the proposed test cannot be used to fulfil information requirement for Annex IX, Section 9.2.1.2, because it addresses aquatic sediments, and not surface water.

However, the proposed OECD 308 test can be used to fulfil the information requirement for Annex IX, Section 9.2.1.4 (sediment simulation testing). Since the substance has a high potential for adsorption (estimated log Koc >5), simulation testing in sediment is required pursuant to Section 9.2.1.4. Therefore, the testing proposal is accepted for this endpoint.

Furthermore, according to Annex IX, Section 9.2.1.3. soil simulation testing is required for substances with a high potential for adsorption to soil, unless direct and indirect exposure of soil is unlikely or the substance is readily biodegradable. Since the substance has a high potential for adsorption (estimated log Koc >5), simulation testing in soil is required pursuant to Section 9.2.1.3. ECHA considers that an Aerobic and anaerobic transformation in soil test, EU C.23/OECD 307 is suitable to fulfil the information requirement.

The Registrant claims that exposure to soil is negligible. In particular he indicates that sewage sludge would not be applied to soil as it would have to be incinerated. However, this claim has not been demonstrated and is not supported by the information available in the dossier. In particular, Part 9 of the Chemical Safety Report (exposure assessment), indicates that for exposure scenarios 2, 3, 4 and 5 application of sewage treatment plant

(STP) sludge on agricultural soil has to be assumed. For scenario 1, manufacture of organic peroxides, the Registrant refers to a municipal STP, and assumes that the sludge is incinerated ("incineration of sewage sludge from exposed STPs is standard practice at manufacturing sites of peroxides"). It is noted that application of municipal sewage sludge to agricultural soil is still practiced in the EU[1]. According to the exposure scenario presented in section 9 of the CSR, most releases will be directed to STP, and based of the estimated log Koc >5, a large proportion of the substance is expected to adsorb onto the STP sludge. STP sludge could eventually be applied to agricultural soils. Since the substance is moreover not readily biodegradable, the information requirement for Annex IX, Section 9.2.1.3. cannot be waived with a reference to column 2.

In addition, the information requirement for Annex IX, Section 9.2.1.2. needs to be fulfilled with a suitable test. ECHA considers that an Aerobic mineralisation in surface water - simulation biodegradation test, EU C.25/OECD 309 is suitable to fulfil the information requirement. In addition, since the substance is soluble to water and since the substance is not readily biodegradable, the information requirement for Annex IX, Section 9.2.1.2. cannot be waived with a reference to column 2. Column 2 indicates that the study does not need to be conducted if the substance is highly insoluble in water or if the substance is readily biodegradable.

The identification of degradation products is a standard information requirement according to Annex IX, Section 9.2.3. However, no information on the degradation products is available. Therefore there is a data gap for Section 9.2.3. that needs to be fulfilled. In addition, adaptation according to Column 2 is not possible, since the substance is not readily biodegradable.

According to Annex XIII, the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions. The substance subject to the present decision is used and released within the context of the REACH Regulation in the EU. Therefore, the Registrant is requested to perform the study at 12 °C (285K) as this temperature is indicated in the Guidance on information requirements and chemical safety assessment Chapter R.16., Table R.16-9 (version 2.1 October 2012) as the average environmental temperature for the EU to be used in the chemical safety assessment. ECHA considers that performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD307 and OECD308 and OECD309.

In his comments, the Registrant agreed to perform a simulation test in sediment (OECD 308), but disagreed with the requests for a simulation test in surface water (OECD 309) and for a simulation test in soil (OECD 307). The Registrant did not provide any objection on the request for information for the identification of degradation products.

ECHA notes that criteria for the identification of persistent (P) or very persistent (vP) substances are detailed respectively in Section 1.1.1. and Section 1.2.1. of Annex XIII of the REACH Regulation. Distinct criteria are defined for water, sediment and soil. A substance is classified as persistent or very persistent if it fulfils respectively the P or vP criterion for any of these environmental compartments. Therefore, the Registrant needs to conclude on P and vP for water, sediment and soil all together. Consequently he shall consider performing simulation tests for these three compartments, unless he can demonstrate that this is not relevant. Column 2 of Section 9.2. of Annex IX of the REACH Regulation specifies that the choice of the appropriate test(s) in appropriate media depends of the results of the CSA. The identified uses and releases patterns as well as the intrinsic properties of the registered substance should be considered when assessing whether a compartment is

[1] See for example: http://ec.europa.eu/environment/waste/sludge/pdf/part_ii_report.pdf

relevant or not. For example a simulation test in a compartment is not needed if it can be demonstrated that neither direct nor indirect exposure occurs in that compartment or if the test is not technically feasible.

The Registrant claimed that exposure to soil was negligible and on this basis disagreed to perform a simulation test in soil (OECD 307). ECHA acknowledges that the sewage sludge is incinerated and not applied to agricultural soil for exposure scenario 1, i.e. manufacturing (ES 1) and therefore that exposure to soil is likely to be negligible for that scenario. For other exposure scenarios (ES 2, 3, 4 and 5), the Registrant claimed that the exposure assessment did not show any risk to soil and that the assessment was based on "*absolute worst-case conditions*". ECHA notes that the exposure assessment does not show that exposure to soil is unlikely. ECHA further notes that the assessment is not based on "*absolute worst-case conditions*" since the Registrant has used an assessment factor lower than recommended in ECHA Guidance R.10 for deriving the PNECs and that for some exposure scenarios he has applied release factors lower than recommended in ECHA Guidance R.16. ECHA considers that the Registrant failed to demonstrate that the soil compartment is not relevant.

The Registrant agreed to perform a simulation test in sediment (OECD 308) and claimed that this test could also fulfil the information requirement of Annex IX, Section 9.2.1.2 of the REACH Regulation (ultimate degradation in surface water). On this basis he disagreed to perform a simulation test in water (OECD 309). ECHA considers that OECD 308 and OECD 309 are two different tests. OECD 309 is relevant to fulfil the information requirement of Annex IX, Section 9.2.1.2. of the REACH Regulation and OECD 308 is relevant to fulfil the information requirement of Annex IX, Section 9.2.1.4. of the REACH Regulation. Contrary to what the Registrant claimed, an OECD 308 test cannot be used to fulfil the information requirement of Annex IX, Section 9.2.1.2. of the REACH Regulation to assess biodegradation in surface water. In an OECD 308 test, complex transfer processes exist between sediment and water. Ultimately, removal from the water phase can be partially due to actual biodegradation but also due to adsorption to sediment. The derivation of degradation half-lives in water from an OECD 308 test is therefore highly uncertain and should not be used for the P/vP assessment in water (see ECHA Guidance on information requirements and chemical safety assessment, Chapter R11, version 2.0, November 2014, Table R.11—5).

The Registrant further indicates that OECD 308 may prove to be technically unfeasible "*in view of the analytical difficulties observed in other studies (see eg hydrolysis study, IUCLID section 5.1.2).*" ECHA acknowledges the analytical difficulties raised by the Registrant but considers that he did not demonstrate that the test was technically unfeasible, as for example radio-labelling of the substance can be used to overcome the analytical difficulties.

The Registrant did not object to the request for information for the identification of degradation products. ECHA notes that information on degradation products is in itself required for the PBT/vPvB assessment as Annex XIII of the REACH Regulation explicitly requires that PBT/vPvB properties of degradation products need to be taken into account. Information on degradation products shall also be taken into account for the exposure assessment (Annex I 5.2.4. of the REACH Regulation) and for the hazard assessment (e.g. see column 2 of Annex X 9.4 and Annex X 9.5.1 of the REACH Regulation). Finally, ECHA further points out that information on degradation products is required for the preparation of Section 12 of the safety datasheet (Annex II of the REACH Regulation).

b) Outcome

Therefore, pursuant to Article 40(3)(c) and (a) of the REACH Regulation, the testing proposal for the test aerobic and anaerobic transformation in aquatic sediment systems simulation biodegradation study (EU C.24/OECD 308) is accepted for the provision of information to fulfil Annex IX, Section 9.2.1.4., while the Registrant is required to carry out the following additional studies using the registered substance subject to the present decision: a) Simulation testing on ultimate degradation in surface water (Annex IX, 9.2.1.2.; test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25/OECD 309); b) Soil simulation testing (Annex IX, Section 9.2.1.3.; test method: Aerobic and anaerobic transformation in soil, EU C.23/OECD 307); c) Including the identification of the degradation products (Annex IX, Section 9.2.3.) by means of one of the above test methods. All these tests have to be carried out at a temperature of 12°C.

Notes for consideration by the Registrant

In accordance with Annex I, Section 4, of the REACH Regulation the Registrant should revise the PBT assessment when results of the test detailed above are available. The Registrant is advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R.11.4. and Figure R.11—3 on the PBT/vPvB assessment for further information on the integrated testing strategy for the persistence assessment of the registered substance. The Registrant should revise the PBT/vPvB assessment when information on persistence is available.

When several compartments are relevant, results from multi-media modelling (e.g. Mackay level III models) can be used to decide which compartment to test first. Difficulties in conducting the test or interpreting its results should also be considered. For example, simulation tests performed in sediment or in soil would possibly imply the formation of non-extractable residues (NER). These residues (of the parent substance and/or degradation products) are bound to the soil or the sediment particles and cannot be extracted using conventional chemical extraction methods. Interpretation of NER is not straightforward and is still a topic of scientific and regulatory debate as there is currently no agreed method to assess NER further. ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.11: PBT/vPvB assessment, Version 2.0 November 2014 states that the formation of NER should be interpreted as removal instead of biodegradation per se but makes clear that removal alone is insufficient for the P/vP assessment (R.11.4.1.1).

IV. Adequate identification of the composition of the tested material

The process of examination of testing proposals set out in Article 40 of the REACH Regulation aims at ensuring that the new studies meet real information needs. Within this context, the Registrant's dossier was sufficient to confirm the identity of the substance to the extent necessary for examination of the testing proposal. The Registrant must note, however, that this information, or the information submitted by other registrants of the same substance, has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In relation to the proposed tests, the sample of substance used for the new studies must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is within the specifications of the substance composition that are given by the joint registrants. It is the responsibility of all joint registrants of the same substance to agree to the tests proposed (as applicable to their tonnage level) and to document the necessary information on their substance composition.

In addition, it is important to ensure that the particular sample of substance tested in the new studies 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 by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new studies must be suitable to assess these grades.

Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the studies to be assessed.

V. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Article 51(8) of the REACH Regulation. Such appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on the ECHA's internet page at http://www.echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

Authorised[2] by Ofelia Bercaru, Head of Unit, Evaluation E3

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