EUROPEAN CHEMICALS AGENCY

Final decision: TPE-D-0000002548-68-06/F Helsinki, 11 March 2013

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

For tetrapropylenebenzene, CAS No 25265-78-5 (EC No 246-772-4), 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 tetrapropylenebenzene, CAS No 25265-78-5 (EC No 246-772-4), by [redacted] (Registrant).

- 90-day oral toxicity study (OECD 408),
- Extended one-generation reproductive toxicity study (OECD guideline for the extended one-generation reproductive toxicity study, Version dated 17 November 2010).

The present decision relates to the examination of the testing proposal for a sub-chronic toxicity study (90-day). The testing proposal for the extended one-generation reproductive toxicity study is addressed in a separate decision although all testing proposals were initially addressed together in the same draft decision.

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 6 September 2012, the date upon which ECHA notified its draft decision to the Competent Authorities of the Member States pursuant to Article 51(1) of the REACH Regulation.

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 present dossier at a later stage.

On 18 April 2011, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of the testing proposals set out by the Registrant in the registration dossier for the substance mentioned above.

ECHA held a third party consultation for the testing proposals from 15 September 2011 until 31 October 2011. ECHA did receive information from third parties (see section III below).

On 06 June 2012 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 04 July 2012 ECHA received comments from the Registrant to ECHA's draft decision requesting extension of the commenting period. The Registrant was given additional period for commenting (until 1 August 2012) provided he submits written evidence of his exceptional situation. On 31 July ECHA received comments from the Registrant requesting further extension of the commenting period. The requested written evidence was not received.

ECHA considered the Registrant's comments received. The draft decision was not amended.

On 6 September 2012 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 to amend the draft decision within 30 days of the receipt of the notification.

Subsequently, Competent Authorities of the Member States submitted proposals for amendment to the draft decision. ECHA reviewed the proposals for amendment received and decided not to amend the draft decision.

On 10 October 2012 ECHA notified the Registrant of proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on those proposals for amendment within 30 days of the receipt of the notification.

On 22 October 2012 ECHA referred the draft decision to the Member State Committee.

On 7 November 2012, the Registrant provided comments on the proposed amendments. The Member State Committee took the comments of the Registrant into account.

The draft decision was split into two draft decision documents: one relating to the testing proposal for an extended one-generation reproductive toxicity study and one relating to the 90-day sub-chronic toxicity study.

A unanimous agreement of the Member State Committee on the draft decision relating to the testing proposals for 90-day sub-chronic toxicity study was reached on 26 November 2012 in a written procedure launched on 14 November 2012. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Testing required

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

- Sub-chronic toxicity study (90-day) in rats, oral route (Annex IX, 8.6.2.; test method: EU B.26/OECD 408). The study protocol shall be modified with additional sperm parameters and histopathological evaluations to evaluate effects on reproductive organs; specifically as described in OECD 416 adopted 22nd January 2001, paragraphs 29-32, 39, 41-45.

The Registrant shall conduct the sub-chronic toxicity study and based on the results consider the possibilities for adaptations of the standard information requirement for the reproductive toxicity according to column 1 or 2 provisions of the relevant Annexes of the REACH Regulation.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **11 September 2014** an update of the registration dossier containing the information required by this decision.

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 and scientific information submitted by third parties.

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 registration dossier contains a short-term repeated dose toxicity study (28 day) which indicated adverse effects on organs, including the reproductive organs. The Registrant has not classified the registered substance in respect of toxicity following repeated exposure, for example, Specific Target Organ Toxicity – Repeated Exposure (STOT-RE) or R48. Since the findings are not sufficient for classification according to STOT-RE or R48 then the criterion specified in Column 2, Annex IX, 8.6.2 for adapting the information requirement for a sub-chronic toxicity study cannot be met. The Registrant has proposed to perform a sub-chronic toxicity study (90-day).

Since the available 28-day toxicity study indicated adverse effects on the reproductive organs, the proposed 90-day toxicity study might give a reliable basis for the Registrant to partially study the potential for adverse effects in respect of the fertility endpoint, and depending on the outcome of the study, consider applying any appropriate classification. To provide such a reliable basis, the study protocol shall be modified to include observations of additional sperm parameters and histopathological examination of the reproductive organs; specifically as described in OECD 416 adopted 22nd January 2001, paragraphs 29-32, 39, 41-45. This modification will generate information that can be relevant to the potential use of a Column 2 adaptation of the standard information requirement of Annex IX, 8.7.3. In the case that adverse effects that meet the criteria for classification for Repr. Cat. 1B are observed in the duly modified 90-day toxicity study, the Registrant is requested to immediately update the dossier with the relevant information and consider the adaptation possibility for the information requirement on reproduction toxicity (point 2 in Section II).

The Registrant proposed testing by the oral route. In the light of the physico-chemical properties of the substance, ECHA considers that testing by the oral route is appropriate.

The Registrant did not specify the species to be tested. According to the test method EU B.26/OECD 408 the rat is the preferred rodent species. ECHA considers this species as being appropriate. To further study the findings seen in repeated dose 28-day oral toxicity study, the Sprague-Dawley strain used in that study should also be used in the repeated dose 90-day oral toxicity study.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation. For the reasons explained further below the information provided by third parties is not sufficient to fulfil this information requirement.

A third party has proposed a strategy for ECHA to consider before further tests on animals are requested. However, third parties were invited, as specified by Article 40(2) of the REACH Regulation to submit "scientifically valid information and studies that address the relevant substance and hazard end-point, addressed by the testing proposal". As the proposal for a strategy as such cannot be regarded information or studies, ECHA concludes that this is not a sufficient basis to fulfil the data/information requirement.

A third party has commented that the registration dossier contains a 28-day toxicity study which indicates treatment-related findings in the male reproductive tract and which may be adequately investigated in the existing two-generation reproductive toxicity study. ECHA notes that – as explained in the Statement of Reasons in the two-generation decision (Section III) (see the following paragraph) - the two-generation reproductive toxicity study has not been performed using the registered substance and is not a sufficient basis to address the specific concern for fertility of the registered substance. Therefore, ECHA concludes that this study cannot on its own fulfil the data/information requirement.

The registration dossier contains a two-generation reproductive toxicity study designated as key study with a reliability of 2. The Registrant indicated that the full details of the report are not available. Furthermore, the Registrant indicated that this study was performed with a mixture of linear decyl- to tridecyl-benzenes and not with the registered substance. Therefore, this study is not a sufficient basis to address the specific concern for fertility of the registered substance and ECHA agrees with the registrant that the available study is not adequate to fulfil the information requirement for a two-generation reproductive toxicity study on the registered substance.

c) Outcome

Therefore, pursuant to Article 40(3)(b) of the REACH Regulation, the Registrant is required to carry out the following study: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD 408) using the registered substance. The study protocol shall be modified with additional sperm parameters and histopathological evaluations to evaluate effects on reproductive organs; specifically as described in OECD 416 adopted 22nd January 2001, paragraphs 29-32, 39, 41-45.

At any time, the Registrant shall take into account that there may be an obligation to make every effort to agree on sharing of information and costs with other Registrants.

d) Deadline for submitting the information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 30 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also requested a two-generation reproductive toxicity study according to the standard information requirement of Annex IX, 8.7.3 of the REACH Regulation. As the testing proposal for this study is not addressed in the present decision, ECHA considers that a reasonable time period for providing the required information in the form of an updated IUCLID5 dossier is 18 months from the date of the adoption of the decision. The decision was therefore modified accordingly.

IV. Adequate identification of the composition of the tested material

The process of evaluation 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 evaluation of the testing proposal. The Registrant must note, however, that this information has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

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. If the registration of the substance covers different grades, the sample used for the new studies must be suitable to assess these.

Finally, there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the study/studies to be assessed.

V. General requirements for the generation of information and Good Laboratory Practice

ECHA reminds registrants of the requirements of Article 13(4) of the REACH Regulation that ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP).

According to Article 13(3) of the REACH Regulation, tests that are required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the European Chemicals Agency as being appropriate. Thus, the Registrant shall refer to Commission Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 as adapted to technical progress or to other international test methods recognised as being appropriate and use the applicable test methods to generate the information on the endpoints indicated above.

VI. 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://echa.europa.eu/appeals/app_procedure_en.asp. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

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Director of Regulatory Affairs