EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000004332-83-03/F Helsinki, 19 June 2014

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

For Reaction mass of 4-tert-butylphenol and 1,3- phenylenedimethanamine and 2-({[3-(aminomethyl) benzyl]amino}methyl)-4-tert-butylphenol, (EC No 939-071-6), 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 Reaction mass of 4-tert-butylphenol and 1,3-phenylenedimethanamine and 2-({[3-(aminomethyl) benzyl]amino}methyl)-4-tert-butylphenol (EC No 939-071-6), submitted by [redacted] (Registrant).

- Subchronic study according OECD Guideline 408 (Repeated Dose 90-Day Oral Toxicity in Rodents) on the registered substance;
- A study according OECD Guideline 414 (Prenatal Developmental Toxicity Study) in rats with the registered substance.

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 March 2014, 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 registration at a later stage.

The examination of the testing proposals was initiated upon the date when receipt of the complete registration dossier was confirmed on 27 May 2013.

ECHA held a third party consultation for the testing proposals from 2 July 2013 until 16 August 2013. ECHA did not receive information from third parties.

On 8 November 2013 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 4 December 2013 ECHA received comments from the Registrant.

The ECHA Secretariat considered the Registrant's comments. The information is reflected in the Statement of Reasons (Section III) whereas no amendments to the Information Required (Section II) were made.

On 6 March 2014 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.

As no proposal for amendment was submitted, ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

II. Testing required

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

1. Sub-chronic toxicity study (90-day) in rats, oral route (Annex IX, 8.6.2.; test method: EU B.26/OECD 408)
2. Pre-natal developmental toxicity study in rats or rabbits, oral route (Annex IX, 8.7.2.; test method: EU B.31/OECD 414).

The Registrant shall determine the appropriate order of the studies taking into account the possible outcome and considering the possibilities for adaptations of the standard information requirements according to the column 2 provisions of the respective Annex and those contained in Annex XI of the REACH Regulation.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **27 June 2016** an update of the registration dossier containing the information required by this decision. The timeline has been set to allow for sequential testing as appropriate.

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.

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.

1. Sub-chronic toxicity study (90-day)

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

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 proposed testing by the oral route. The registered substance is a liquid with a low vapour pressure (0.16 Pa) classified as corrosive to skin and eyes. Several PROCs like PROC 7 (industrial spraying), 8 and 9 (transfer of the substance), 10 (roller application or brushing), 11 (non-industrial spraying) indicate potential inhalation exposure. Spray application is mentioned in the CSR with concentrations of the substance in the product of up to [redacted]%, less than [redacted]% and less than [redacted]%. The Registrant did not derive a long-term DNEL for inhalation long-term local effects but addressed the risk for respiratory tract irritation via a qualitative assessment. Since the risk for respiratory tract irritation is addressed by the Registrant and the short-term repeated dose toxicity study (28 days) was performed via the oral route, ECHA agrees with the Registrant that testing by the oral route is most appropriate.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD 408) using the registered substance.

2. Pre-natal developmental toxicity study

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 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 did not clearly specify the species to be used for testing. ECHA notes that in the further specifications the Registrant assumes testing on rabbits, which is however not clearly part of his proposed testing.

The Registrant proposed testing by the oral route. 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.

ECHA notes that the Registrant mentions in the dossier that the proposed exposure duration would be from gestation day 6 through 18 which coincides with the organogenesis period in rabbits. However, ECHA notes that he has not justified this part of his testing proposal. ECHA furthermore notes that the test method EU B.31/OECD 414 is not intended to examine solely the period of organogenesis (e.g. days 5-15 in the rodent, and days 6-18 in the rabbit) but is designed to investigate also effects from preimplantation through the entire period of gestation to the day before caesarean section in order to properly cover the information requirements for this endpoint. Therefore, a test which only looked at the period of organogenesis would be incompliant with the test method for EU B.31/ OECD 414, unless there was an adequate justification for that deviation. Following the submission of the draft decision, the Registrant proposed in his comments two more exposure days (G.D. 6-20 instead of 6-18) to the time initially proposed for exposure. However, the new exposure time still does not cover the effects from preimplantation, there is not an adequate justification for this deviation from the test method, and ECHA considers that the proposed exposure time would be incompliant with test method EU B.31/ OECD 414. Therefore, while

ECHA approves the proposed test method, it does not approve the proposed exposure duration. The choice of the appropriate exposure duration in principle remains possible. It is however under the responsibility of the Registrant. He would have to ensure and document that the key parameters of the information requirement in question are fulfilled by the study.

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

3. Request for deadline extension

In their comments to the draft decision, the Registrant argued that taking into account that a dose-range finding study will need to be conducted prior to the OECD 414 prenatal developmental toxicity study, a timeframe of 36 to 48 months would be required. ECHA notes that in absence of adequate documentation of specific justifications, an extension of the standard timeline is not deemed justified and hence ECHA decided not to grant such an extension.

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 proposals. The Registrant must note, however, that this information 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 grade(s) registered to enable the relevance of the 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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Leena Ylä-Mononen
Director of Evaluation