EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002224-84-03/F Helsinki, 25 July 2012

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

**For 2,5-di-tert-pentylhydroquinone, CAS No 79-74-3 (EC No 201-222-2), 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 a testing proposal set out in the registration dossier for 2,5-di-tert-pentylhydroquinone, CAS No 79-74-3 (EC No 201-222-2), submitted by [redacted] (Registrant), latest submission number [redacted], for 100 to 1000 tonnes per year.

In accordance with Articles 10(a)(ix) and 12(1)(d) of the REACH Regulation, the Registrant submitted the following testing proposal as part of the registration dossier to fulfil the information requirements set out in Annex IX:

- 90-day oral toxicity study (OECD 408) in rodents (rats), oral route

The examination of the testing proposals was initiated on 22 November 2010.

ECHA opened a third party consultation for the testing proposals including testing on vertebrate animals that was held from 31 May 2011 until 15 July 2011. ECHA did receive information from third parties (see section III below).

On 5 January 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.

By 6 February 2012 the Registrant did not provide any comments on the draft decision to ECHA.

On 2 March 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 did not propose amendments to the draft decision and ECHA took the decision pursuant to Article 51(3) 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 requirements of the REACH Regulation. The decision does not prevent ECHA to initiate a compliance check on the present dossier at a later stage.

II. Testing required

Pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant shall carry out the following proposed test using the indicated test method on the registered substance:

- Sub-chronic toxicity study (90-day) in rats, oral route (Annex IX, 8.6.2., test method: EU B.26/OECD 408).

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **27 January 2014** an update of the registration dossier containing the information required by this decision.

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 proposal submitted by the Registrant for the registered substance and scientific information submitted by third parties.

Sub-chronic toxicity study (90-day)

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 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 generate the data for this endpoint.

The Registrant proposed testing by the oral route. In the light of the physico-chemical properties of the substance and the information provided on the uses and human exposure, ECHA considers that testing by the oral route is appropriate. Specifically, the vapour pressure of the substance is low, indicating low potential for exposure to vapours of the substance. The information on granulometry indicates that 73.5% of the substance has a particle size under 40 µm, which indicates the particles are inhalable, however there is no information showing the presence of respirable particles below 5 µm in the substance. In addition, there is no toxicological information indicating the substance shows toxicity specific to a particular route of exposure. Finally, according to the ECHA Guidance on information requirements, (R.7a,p.329) the oral route is the preferred route of exposure for repeated dose toxicity testing, and there is no information indicating that another route should be used in this case.

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.

b) Consideration of third party information

ECHA received third party information concerning the testing proposal during the public 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 that before an oral sub-chronic toxicity study (OECD Guideline 408) is conducted, consideration should be given to the following weigh of evidence arguments :

1. Evaluate the need to conduct a 90-day sub-chronic toxicity study (OECD Guideline 408) in light of the results of the existing oral 28-day sub-chronic toxicity study (OECD Guideline 407), the existing chronic toxicity study, and other toxicological data on the substance and on analogues quinones.
2. Consult (QSAR) expert systems
3. Exposure considerations use the TTC for repeated dose endpoint.

In generally the 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. Specifically, regarding each point, ECHA concludes the following:

1. The sub-chronic repeated dose toxicity study (90 day) is a standard information requirement according to Annexes IX, 8.6.2. of the REACH Regulation. The information provided by the third party does not meet the specific rules for adaptation of the information requirement for repeated dose toxicity under column 2 of Annex IX, 8.6. Specifically the available data on repeated dose toxicity do not show severe toxicity according to the criteria for classifying the substance as R48 and the existing chronic study is inadequate. Therefore, the third party proposal does not provide sufficient basis to fulfil the data/information requirement In addition, the third party provides information on existing data on the substance 3- ter-butyl-4-hydroxyasnisole. However, the third party does not provide a justification, in accordance with Annex XI, Section 1.5. of the REACH Regulation, as to why the information from this substance is applicable for the registered substance. Therefore, ECHA concludes that testing cannot be omitted based on this information.

2. The third party provided the results of QSAR profiling using OECD Toolbox 2.0, which shows DNA binding attributed to quinone-type chemicals, but no alerts for the micronucleus assay or mutagenicy carcinogenicity be Benigni/Bossa. However, the third party provides no justification for why this information could be used to adapt the standard information requirement for a 90 day repeated dose toxicity study, and the QSAR results do not address the proposed test. Therefore, ECHA concludes that testing cannot be omitted based on this information.

3. The third party states that since testing can be exempted based on negligible exposure, exposure should be thoroughly analysed before conducting the test. In addition, they suggest that the Threshold of Toxicological Concern (TTC) concept should be adopted and cut-off values (human exposure threshold values below which there is no significant risk to human health) for oral (1.5/9/30 µg/kg bw/day)

exposure should be used. According to Annex XI, Section 3 of the REACH Regulation, the testing can be omitted if it can be demonstrated that there is no or no significant exposure. The Registrant did not use substance-tailored exposure-driven testing according to Annex XI, Section 3 for this endpoint, but indicated that for several uses, the opportunity for exposure arises. Therefore, ECHA concludes that testing cannot be omitted based on negligible exposure.

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

ECHA always 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). National authorities monitoring GLP maintain lists of test facilities indicating the relevant areas of expertise of each facility.

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.

National authorities monitoring good laboratory practice (GLP) maintain lists of test facilities indicating the relevant areas of expertise of each facility.

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://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.

[redacted]

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Director of Regulatory Affairs