Decision number: TPE-D-2114321172-66-01/F Helsinki, 11 March 2016

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

For biphenyl-4,4'-diol, EC No 202-200-5(CAS No 92-88-6), 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 jointly submitted registration dossier in accordance with Articles 10(a)(ix) and 12(1)(d) thereof for biphenyl-4,4'-diol, EC No 202-200-5 (CAS No 92-88-6), submitted by [redacted] (Registrant).

- 90-day oral toxicity study (OECD 408) in rats, oral route.
- Developmental toxicity / teratogenicity study (OECD 414).

This decision is based on the registration 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 13 October 2015, i.e. 30 calendar days after the end of the commenting period.

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 testing proposals for further examination pursuant to Article 40(1) on 25 April 2013. The registration was subsequently updated on 13 May 2013 containing the above-mentioned testing proposals.

ECHA held a third party consultation for the testing proposals from 15 July 2014 until 29 August 2014. ECHA received information from third parties (see section III below).

On 4 August 2015 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 26 August 2015 ECHA received comments from the Registrant on the draft decision.

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 21 January 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.

As no proposal for amendment was submitted, ECHA took the decision pursuant to Article 51(3) 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. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26/OECD 408) in rats;
2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31/OECD 414) in rats or rabbits, oral route.

Notes 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 request(s) in this decision, or to fulfil otherwise the information requirement(s) 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 **19 March 2018** 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 and scientific information submitted by third parties.

A. Tests required pursuant to Article 40(3)

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

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 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) in rats via the oral route (EU B.26/OECD 408) with the following justification: *"(enhanced OECD 408) is proposed in order to meet the data requirements specified in Column 1 of Annex IX of the REACH Regulation. Testing is subject to confirmation by ECHA".* The Registrant additionally indicated that *"It is envisaged that the 90-day study design incorporates additional endpoints of relevance to reproductive toxicity."*

ECHA considers that the proposed study, via the oral route is appropriate to fulfil the information requirement of Annex IX, Section 8.6.2. of the REACH Regulation because the proposed route is the most appropriate route of administration having regard to the likely route of human exposure due to the following reasons:

After balancing considerations related to the properties of the substance (namely solid state which does not exert skin or eye irritation/corrosion), there was no systemic effect on the GI tract after oral exposure in 28d RDT study, whereas other effects (urinary turbidity, effects on liver) were observed demonstrating bioavailability of the substance after oral administration. The information provided on the uses and human exposure (no uses with spray application), indicate that testing by the oral route is most appropriate.

The Registrant proposed testing in rats. 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.

The REG did not indicate the test material. ECHA requests that the test is performed on the registered substance.

The Registrant proposed to extend the sub-chronic toxicity study (90 day) by including additional examinations/parameters. ECHA notes, that it is at the Registrant's discretion to perform the intended additional examinations during the testing program and use the results to ensure the safe use of the substance. However, the Registrant is reminded that the proposed extension of the study presently requested does not fulfil the standard information requirement in the registration dossier for reproductive toxicity set out in Annex IX, Section 8.7.3.

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 that "*read across - using Hydroquinone (EC 204-617-8) and Biphenyl (EC 202-163-5)*" is to be considered, and advises to "*see registration Hydroquinone (EC 204-617-8) and Biphenyl (EC 202-163-5)*".
The third party bases his comment on existing data for 2 analogue substances, which have been registered under REACH. ECHA acknowledges that the third party has proposed an adaptation argument relying on a read across approach for the Registrant to consider.

The data on which the argument relies on has not been made available to ECHA or the Registrant, namely no robust study summary has been submitted which can be assessed pursuant to the criteria of Annex XI, section 1.5. In addition the third-party has not submitted any read-across justification which would fulfil the requirement for adequate and reliable documentation laid out in Annex XI, section 1.5.
Hence the information provided by the third party is insufficient for demonstrating that the conditions of Annex XI, Section 1.5. of the REACH Regulation are met. For example, the registrant should access the robust study summary in order to assess whether the possible adaptation holds, and should also develop a read-across argumentation that would be acceptable to ECHA. Therefore, the information provided by the third party in itself is not sufficient to adapt the standard information requirement.

ECHA notes that it is the Registrant's responsibility to consider and justify any adaptation of the information requirements in accordance with the relevant conditions as established in Annex XI, Section 1.5. Therefore, the Registrant may assess whether he can justify a read-across as suggested by the third party. If the information requirement can be met by way of adaptation, the Registrant may include the adaptation argument with all necessary documentation according to Annex XI, Section 1.5. in an updated registration. The Registrant is reminded that this decision does not take into account any updates of the registration submitted later than the date indicated in Section I of this decision. Later updates of the registration will however be examined in the follow-up evaluation pursuant to Article 42 of the REACH Regulation.

However, ECHA notes that the information provided by the third party is insufficient for demonstrating that the conditions of Annex XI, Section 1.5. of the REACH Regulation are met. Therefore, the test proposed by the Registrant is adequate to fulfil the information requirements.

The Registrant commented on third party information stating that "*The "Registrant" has been notified by the "Agency" of a third party proposal to consider read-across to Hydroquinone (EC 204-617-8) and Biphenyl (EC 202-163-5). Neither robust study summary nor read-across justification has been provided by the third party. Therefore, the information provided is not sufficient to adapt the dossier. Despite this lack of information, a preliminary assessment of the relevance of the read-across has been performed, based on data publically available (i.e. disseminated dossier of the read-across substance in ECHA disseminated website). This screening has not shown any scientifically relevant rationale to cover both endpoints (reproduction toxicity and developmental toxicity) by read-across to the proposed substances*".

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

The Registrant commented on the draft decision, providing additional rationale for the approach originally set out in the testing proposal for 90-day toxicity which is to carry out "*additional examinations on the reproductive organs and tissues with the objective of addressing sufficiently the potential concerns on reproductive toxicity*". ECHA has considered these comments, and maintains the position set out in the draft decision, i.e. that it is at the Registrant's discretion to perform the intended additional examinations during the testing program and use the results to ensure the safe use of the substance, and that the Registrant is reminded that the proposed extension of the study presently

requested does not fulfil the standard information requirement in the registration dossier for reproductive toxicity set out in Annex IX, Section 8.7.3. ECHA notes the Registrant's agreement to conduct the test as proposed in the draft decision.

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

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 in rats according to EU B.31/OECD 414 with the following justification: *"A study of developmental toxicity in the rat using oral dosing is planned (OECD 414); the testing proposal is subject to confirmation by ECHA. It is envisaged the 90-day study design incorporates additional endpoints of relevance to reproductive toxicity".*
The REG did not indicate the test material. ECHA requests that the test is performed on the registered substance.

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 proposed testing in rats and 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. Since the substance is a solid and systemic effects have been observed in the oral RDT-28 study, there is no indication which would justify deviating from the default route and the oral route is considered appropriate. Testing should be performed by the oral route with the rat or the rabbit as a first species to be used. The reference to *"the Registrant proposed to extend the sub-chronic toxicity study (90 day) by including additional examinations/parameters"* has been addressed under section III. 1.a of the present decision.

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 that "*read across - using Hydroquinone (EC 204-617-8) and Biphenyl (EC 202-163-5)*" is to be considered, and advises to "*see registration Hydroquinone (EC 204-617-8) and Biphenyl (EC 202-163-5)*".

The third party bases his comment on existing data for 2 analogue substances, which have been registered under REACH. ECHA acknowledges that the third party has proposed an adaptation argument relying on a read across approach for the Registrant to consider.
The data on which the argument relies on has not been made available to ECHA or the Registrant, namely no robust study summary has been submitted which can be assessed pursuant to the criteria of Annex XI, section 1.5. In addition the third-party has not submitted any read-across justification which would fulfil the requirement for adequate and reliable documentation laid out in Annex XI, section 1.5.

Hence the information provided by the third party is insufficient for demonstrating that the conditions of Annex XI, Section 1.5. of the REACH Regulation are met. For example, the registrant should access the robust study summary in order to assess whether the possible adaptation holds, and should also develop a read-across argumentation that would be acceptable to ECHA. Therefore, the information provided by the third party in itself is not sufficient to adapt the standard information requirement.

ECHA notes that it is the Registrant's responsibility to consider and justify any adaptation of the information requirements in accordance with the relevant conditions as established in Annex XI, Section 1.5. Therefore, the Registrant may assess whether he can justify a read-across as suggested by the third party. If the information requirement can be met by way of adaptation, the Registrant may include the adaptation argument with all necessary documentation according to Annex XI, Section 1.5. in an updated registration. The Registrant is reminded that this decision does not take into account any updates of the registration submitted later than the date indicated in Section I of this decision. Later updates of the registration will however be examined in the follow-up evaluation pursuant to Article 42 of the REACH Regulation.

However, ECHA notes that the information provided by the third party is insufficient for demonstrating that the conditions of Annex XI, Section 1.5. of the REACH Regulation are met. Therefore, the test proposed by the Registrant is adequate to fulfil the information requirements.

c) 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).

The Registrant commented on the draft decision. ECHA notes the Registrant's agreement to conduct the test as proposed in the draft decision.

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[1] by Ofelia Bercaru, Head of Unit, Evaluation E3

[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.