EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000004548-66-03/F Helsinki, 12 June 2014

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

For 6'-(dibutylamino)-3'-methyl-2'-(phenylamino)spiro[isobenzofuran-1(3H),9-(9H)-xanthen]-3-one, CAS No 89331-94-2 (EC No 403-830-5), 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 proposal submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12(1)(d) thereof for 6'-(dibutylamino)-3'-methyl-2'-(phenylamino)spiro[isobenzofuran-1(3H),9-(9H)-xanthen]-3-one, CAS No 89331-94-2 (EC No 403-830-5), submitted by [redacted] (Registrant).

- 90-day oral toxicity study (OECD 409) in non-rodents.

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 proposal was initiated upon the date when receipt of the complete registration dossier was confirmed on 17 July 2013.

ECHA held a third party consultation for the testing proposal from 2 September until 18 October 2013. ECHA did receive information from third parties (see section III below).

On 28 November 2013 ECHA sent the draft decision to the Registrant and invited him to provide comments within 45 days of the receipt of the draft decision.

By 13 January 2014 the Registrant did not provide any comments on the draft decision to ECHA.

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 modified test pursuant to Article 40(3)(c) 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)

while the originally proposed test for a 90-day oral toxicity study in non-rodents (test method: EU B.27/OECD 409) proposed to be carried out using the registered substance [6'-(dibutylamino)-3'-methyl-2'-(phenylamino)spiro[isobenzofuran-1(3H),9-(9H)-xanthen]-3-one] is rejected pursuant to Article 40(3)(d) of the REACH Regulation.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **21 December 2015** 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)(c) of the REACH Regulation, ECHA may 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 of the REACH Regulation.

A sub-chronic toxicity study (90 day) one species, rodent, male and female, most appropriate route of administration, having regard to the likely route of human exposure 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.

ECHA understands that the Registrant proposed testing in non-rodents according to the OECD test guideline 409 foreseen for non-rodents. The Registrant did not provide justification for the choice of the test method or the species. Annex IX, section 8.6.2 requires a sub-chronic toxicity study (90-day) in rodent. 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 Registrant proposed testing by the oral route. In light of the physico-chemical properties of the substance (solid not classified as corrosive/irritating to the skin or damaging/irritating to the eyes) and the information provided on the uses and human exposure ECHA considers that testing by the oral route is most appropriate.

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.

Third party information:

A third party has proposed a weight-of evidence approach for ECHA to take into account before further tests on vertebrate animals are required. As part of this approach, the third party *"referred to physicochemical, QSAR and existing toxicity data which clearly indicate that the substance is not absorbed in the gastrointestinal tract and systemic exposure after ingestion does not occur. Performing the proposed 90-day toxicity study is not scientifically justified and additionally is not in the interest of animal welfare"*. 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 information requirement.

ECHA has taken the information provided into account and concludes that it is insufficient for demonstrating that the conditions of Annex XI, Section 1.2, 1.3 and 1.5 of the REACH Regulation are met. More specifically, the proposed weight-of-evidence approach is not sufficient to assume that the substance has or has not a particular dangerous property after sub-acute (28-day) administration of the substance and that the standard information requirement for a sub-chronic toxicity study (90-day) could be adapted. Furthermore, the proposed read-across approach as an element of the weight of evidence justification did not demonstrate that human health effects of the registered substance may be predicted from data on the reference substance. Furthermore, the justification provided by the third party for adapting the study (*"The substances in this group are of very low acute toxicity..."*) does not meet the criteria of column 2 in Annex IX, section 8.6.2. Therefore ECHA concludes that this is not a sufficient basis to fulfil the information requirement.

Although ECHA recognises that the information as provided by the third party might be scientifically valid, it does not fulfil Annex XI requirements and is therefore not sufficient to allow ECHA to reject the testing proposal. Nevertheless, ECHA acknowledges that the Registrant may himself supplement under its own responsibility the argumentation and information provided by the third party in order to make use of adaptation possibilities. This would require that the Registrant documents, using several independent sources of information, that there is a sufficient weight of evidence leading to the assumption/conclusion that a substance has or has not particular dangerous properties, according to the criteria laid down in Annex XI of the REACH Regulation.

c) Outcome

Therefore, pursuant to Article 40(3)(c) 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 [6'-(dibutylamino)-3'-methyl-2'-(phenylamino)spiro[isobenzofuran-1(3H),9-(9H)-xanthen]-3-one].

IV. Adequate identification of the composition of the tested material

It is important to ensure that the particular sample of substance tested in the new study 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 study must be suitable to assess these.

Furthermore, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the study 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://www.echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

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