EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114331778-40-01/F Helsinki, 18 May 2016

DECISION ON 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, EC No 403-830-5(CAS No 89331-94-2), 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 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, EC No 403-830-5 (CAS No 89331-94-2), submitted by [redacted] (Registrant).

- Bioaccumulation test according to OECD Guideline 305 (Bioconcentration: Flow-through Fish Test). The Registrant has indicated his preference for the dietary route of exposure.

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 16 November 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.

The examination of the testing proposal was initiated upon the date when receipt of the complete registration dossier was confirmed on 16 March 2015.

ECHA held a third party consultation for the testing proposal from 12 June until 27 July 2015. ECHA did not receive information from third parties.

On 8 September 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 14 October 2015 ECHA received comments from the Registrant on the draft decision. The ECHA Secretariat considered the Registrant's comments. On basis of this information, only the deadline in Section II was amended. The information is reflected in the Statement of Reasons (Section III).

On 3 March 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 modified test pursuant to Article 40(3)(b) and 13(4) of the REACH Regulation using the indicated test method and the registered substance subject to the present decision:

1. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method Bioaccumulation in Fish: Aqueous and Dietary Exposure, OECD 305). The choice of the route is to be justified, as indicated in Section III below.

Note 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 in this decision, or to fulfil otherwise the information requirement 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 **25 September 2017** an update of the registration dossier containing the information required by this decision, including, where relevant, an update of the Chemical Safety Report.

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.

A. Tests required pursuant to Article 40(3)

1. Bioaccumulation in aquatic species, preferably fish (Annex IX, Section 9.3.2.)

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.

"Bioaccumulation in aquatic species, preferably fish" is a standard information requirement as laid down in Annex IX, Section 9.3.2. 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 testing the registered substance for bioaccumulation in aquatic species (Bioconcentration: Flow-through Fish Test, OECD 305). ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 9.3.2. of the REACH regulation and notes that the currently used OECD protocol (adopted on 2 October 2012) is OECD 305: Bioaccumulation in Fish: Aqueous and Dietary Exposure.

The dossier also includes a QSAR (BCFBAF v3.01) prediction, as well as a 1993 experimental bioaccumulation study that "*did not reach a steady-state of accumulation after 28 days (95% steady state being predicted after 48 days) and it is not possible therefore to classify the test substance as B or vB. It is therefore classified as unassignable Klimisch 4*". ECHA agrees that the existing experimental study in the dossier is not acceptable as the bioconcentration factor (BCF) has been calculated from the water and fish tissue concentrations at a non steady-state conditions.

Regarding the testing proposal in the technical dossier, the Registrant indicated that "*the route of administration will be dietary to overcome the problems experienced of dissolving, and maintaining concentrations of the substance in water*".

ECHA notes however that there are several reasons why the aqueous exposure route may be preferable, in this case, as described below.

Generally, due to problems related to the interpretation of the dietary test results, the Guidance on information requirements (Chapter R.11: PBT/vPvB assessment, Version 2.0, November 2014) advises the use use of the aqueous exposure route: "*For strongly hydrophobic substances (Log Kow > 5 and a water solubility below ~ 0.01-0.1 mg/L), testing via aqueous exposure may become increasingly difficult. However, an aqueous exposure test is preferred for substances that have a high Log Kow but still appreciable water solubility with respect to the sensitivity of available analytical techniques, and for which the maintenance of the aqueous concentration as well as the analysis of these concentrations do not pose any constraints.*"

The registered substance has a high Log Kow, as the Registrant reports the experimental LogKow>4.66. However, ECHA notes that there is also an endpoint study record available in IUCLID Section 5.3.1. that mentions the Log Kow value of 4.4. Additionally, ECHA notes that aqueous exposure should be feasible, as indicated from the performance of the long-term *daphnia* test present in the technical dossier. For example, the *daphnia* test results indicate that the maintenance and the analysis of the low test substance concentration applicable to be used in the bioaccumulation aqueous test might not pose problems. Furthermore, using the aqueous route of exposure would also allow the direct calculation of the BCF and no extrapolation from the biomagnification factor obtained via dietary route would be required.

For the selection of the appropriate exposure route for the test, the Registrant is advised to consult the OECD 305 Test Guideline (2 October 2012) and the ECHA Guidances on information requirements and chemical safety assessment (version 1.1., November 2012), Chapter R7c, (Section R.7.10.3) and (version 2.0, 20140, Chapter R.11, (Section R.11.4.1.2).

The Registrant is also recommended to consider the relevant physical-chemical properties and exposure potential of the registered substance and to justify its route selection. If the aqueous route is preferred, due consideration needs to be given, for example, to the length of the uptake phase in order to ensure conclusive results from the vertebrate animal study.

In the comments to the draft decision the Registrant agreed with the information requirement in the draft decision. Regarding a selected exposure route, the Registrant stated "The final decision on exposure route will be fully justified".

Finally, ECHA reminds that the Chemical Safety Assessment including the PBT/vPvB assessment should also be updated based on the results of the new study and the Registrant should submit a revised Chemical Safety Report.

b) Outcome

Therefore, pursuant to Article 40(3)(b) of the REACH Regulation, the Registrant is required to carry out the proposed study using the registered substance subject to the present decision: Bioaccumulation in aquatic species (Annex IX, 9.3.2.; test method: Bioaccumulation in Fish: Aqueous and Dietary Exposure, OECD 305). The choice of the route is to be justified.

2. Deadline for submitting the required information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 9 months from the date of adoption of the decision. In his comments on the draft decision, the Registrant stated the following: "[...] *However, the registrant believes that more time will be required in the worst case that aqueous exposure is undertaken and respectfully requests an extension of this timeline from 9 months to 20 months. The laboratory that is to undertake the study has reviewed the original bioaccumulation study performed on this substance and notes that for 28 day exposure/14 day depuration, 95% steady-state was predicted to be 48 days and the half-life 11 days which suggests that somewhere close to 60 days would be required for the exposure phase and 60-120 days for the depuration phase. Technical difficulties are expected because, in the original study, tank water concentrations of total radioactivity were not maintained at the high exposure level and the test substance was only approximately 70% of radioactivity in water at day 28 (i.e. the test substance was less than half the target concentration). In addition to this, the solvent used was acetone + 1% Tween 80 which further complicates the study because acetone promotes algae growth. Metabolite identification work may also be required. Given all these factors, this will not be an easy study to conduct to comply with the current guideline and we anticipate that a realistic time frame for this work is 4 months for radiolabel preparation, 12 months test phase, 2 months reporting phase and 2 months for dossier update, CSR revision and dossier submission (20 months total).* [...]" ECHA requested the Registrant to proivde a full justification and all available and transparent documentation for the timeline extension request, but the Registrant did not submit anything. ECHA agrees that the bioaccumulation study will very likely require long uptake and duration periods, based on 1) the substance properties and 2) the results of the reported bioaccumulation study (Bioaccumulation: aquatic, HLS, 1993; disregarded study due to not reaching steady state during testing). However, ECHA concludes – based on the information submitted by the Registrant in his comments and the substance properties and in consideration of previous cases – that a reasonable time period for providing the required information in the form of an updated IUCLID dossier is 16 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 examination of testing proposals set out in Article 40 of the REACH Regulation aims at ensuring that the new study meets 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 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 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.

Finally, 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. 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 Guilhem de Seze, Head of Unit, Evaluation E1

[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.