EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000003220-91-05/F Helsinki, 11 October 2013

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

For 3,6-bis-biphenyl-4-yl-2,5-dihydropyrrolo[3,4-c]pyrrole-1,4-dione, CAS No 88949-33-1 (EC No 413-920-6), 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 proposal submitted as part of the registration dossier in accordance with Article 12(1)(c) thereof for 3,6-bis-biphenyl-4-yl-2,5-dihydropyrrolo[3,4-c]pyrrole-1,4-dione ([redacted]), CAS No 88949-33-1 (EC No 413-920-6), by [redacted] (Registrant).

- Extended one-generation reproductive toxicity study (OECD 443) proposed to be carried out with analogue substance 3,6-bis(4-tert-butylphenyl)-2,5-dihydropyrrolo[3,4-c]pyrrole-1,4-dione ([redacted]), CAS No 84632-59-7 (EC No 416-250-2) (Annex VIII, 8.7)

This decision is based on the registration dossier as submitted with submission number [redacted], for the tonnage band of 10 to 100 tonnes per year. This decision does not take into account any updates after 8 March 2013, 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 2012.

ECHA held a third party consultation for the testing proposal from 25 September 2012 until 12 November 2012. ECHA did receive information from third parties (see section III below).

On 7 January 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.

By 7 February 2013 the Registrant did not provide any comments on the draft decision to ECHA.

On 8 March 2013 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, one Competent Authority of a Member State submitted a proposal for amendment to the draft decision.

On 11 April 2013 ECHA notified the Registrant of the proposal for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on the proposal for amendment within 30 days of the receipt of the notification.

ECHA reviewed the proposal for amendment received and decided not to amend the draft decision.

On 22 April 2013 ECHA referred the draft decision to the Member State Committee.

The Registrant did not provide any comments on the proposed amendment.

After discussion in the Member State Committee meeting on 11-14 June 2013, a unanimous agreement of the Member State Committee on the draft decision as modified in the meeting was reached on 11 June 2013. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Outcome of the testing proposal examination

The testing proposal is rejected pursuant to Article 40(3)(d) of the REACH Regulation.

III. Statement of reasons

Pursuant to Article 40(3)(d) of the REACH Regulation, ECHA may reject a proposed test.

The decision of ECHA is based on the examination of the testing proposal submitted by the Registrant for the registered substance on the proposed analogue substance 3,6-bis(4-tert-butylphenyl)-2,5-dihydropyrrolo[3,4-c]pyrrole-1,4-dione ([redacted]), CAS No 84632-59-7 (EC No 416-250-2), the submitted read-across justification documents and the data matrices therein and scientific information submitted by third parties.

With respect to the testing proposal subject to present decision, the Registrant has proposed to use a read-across and grouping approach, in accordance with Annex XI, 1.5 of the REACH Regulation, and to perform further testing in form of an extended one-generation reproductive toxicity study (OECD 443) on the analogue substance 3,6-bis(4-tert-butylphenyl)-2,5-dihydropyrrolo[3,4-c]pyrrole-1,4-dione ([redacted]), CAS No 84632-59-7 (EC No 416-250-2). To the extent that the proposed testing relies upon a read-across hypothesis, ECHA has considered first the documentation and scientific validity of the proposed read-across approach (Section 1, below), before assessing the testing proposed (Section 2, below).

1. Read-across approach

Article 13(1) of the REACH Regulation requires information on intrinsic properties of substances on human toxicity to be generated whenever possible by means other than vertebrate animal tests, including information from structurally related substances (grouping or read-across), "*provided that the conditions set out in Annex XI are met*".

The evaluation by ECHA of testing proposals submitted by registrants aims at ensuring that generation of information is tailored to real information needs. More specifically, Section 1.5 of Annex XI of the REACH Regulation sets out the conditions to be met by alternative methods so that equivalent results to the prescribed test may be obtained. To this end, it is necessary to consider whether programmes of testing proposed by registrants are appropriate to fulfil the relevant information requirements and to guarantee the identification of health and environmental hazards of substances. In that respect, the REACH Regulation aims at promoting wherever possible the use of alternative means, as long as equivalent results of the prescribed test are provided on health and environmental hazards that meet the relevant information requirement.

In the present case, ECHA considers that the read-across approach proposed by the Registrant, does not give scientific justification on how the relevant toxicological properties of the registered substance can be predicted from the results of the proposed test with an analogue substance. More specifically, Section 1.5 of Annex XI of the REACH Regulation sets out the conditions to be met by alternative methods so that information requirements will be considered to be met. At present, the test proposed by the registrant does not fulfil those conditions, both in relation to the scientific rationale of the read-across approach and to the documentation provided.

In order to apply grouping of substances and read-across approach according to section 1.5 of Annex XI it is required that "*physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity*" (emphasis added). It is a further requirement of Annex XI, 1.5, that "*adequate and reliable documentation of the applied method shall be provided.*"

ECHA Guidance R.6.2 and Section R.6.2.3.1 Stepwise procedure for applying read-across within the analogue approach of ECHA guidance "R.6 QSARS and grouping of chemicals" sets out elements that must be addressed to read-across hypothesis. The read-across hypothesis explains why the properties of a substance may be predicted from another substance for the endpoint concerned.

The Registrant has justified the read-across approach with the document "*Analogue evaluation of the two Diketopyrrolo-pyrrole pigments* [redacted] *and* [redacted] *justifying read-across"* attached in IUCLID Section 13. In that document the Registrant has included a data matrix summarising the molecular structures, physico-chemical properties, environmental fate, exotoxicological information and toxicological information of the two substances subject to the proposed read-across approach. The Registrant argues that the two substances differ only as regards the hydrocarbon groups that are attached to the diketopyrrolo-pyrrole (DDP) core structure and that the (eco-)toxicological properties are dictated by the core DPP structure. The Registrant further argues that the data matrix shows that the physico-chemical and (eco-)toxicological properties are similar between the two substances thus supporting the read-across approach.

ECHA notes that, although the two substances indeed share the DDP structure, they have markedly different hydrocarbon groups (tertiairy butyl versus phenyl) attached to this core structure. The testing proposal concerns reproductive toxicity and the data matrix does not include a data point for this endpoint for the registered substance. ECHA notes that for reproductive toxicity, the proposed analogue substance has shown adverse effects.

The Registrant has not justified why the presumed absence of toxicological effects for the proposed analogue and registered substance observed for other human toxicological endpoints or the similarity of physico-chemical properties between the two substances would allow concluding that the structural difference between the two substances would not influence the reproductive toxicity properties.

ECHA thus concludes that the Registrant has not demonstrated that the human health effects concerning reproductive toxicity of the substance subject to the present decision can be predicted from data on the proposed analogue substance and that the read-across hypothesis is not adequately and reliably justified and documented. Hence the requirements of Annex XI section 1.5 are not met.

Pursuant to Article 40(3)(d) of the REACH Regulation, ECHA rejects the proposal to carry out the test on a substance other than the registered substance. Nevertheless, it is necessary to consider whether the test proposed shall be performed in order to meet the information requirements.

2. Extended one-generation reproductive toxicity study

a) Examination of the testing proposal

Pursuant to Article 40(3)(d) of the REACH Regulation, ECHA may reject a proposed test.

The Registrant has provided in the registration dossier a reproduction/developmental toxicity screening test (OECD 421) performed with the analogue substance 3,6-bis(4-tert-butylphenyl)-2,5-dihydropyrrolo[3,4-c]pyrrole-1,4-dione ([redacted]), CAS No 84632-59-7 (EC No 416-250-2) and not with the registered substance. The Registrant has considered that the results of that study trigger a need to perform further reproductive toxicity study already at Annex VIII level, i.e. on a tonnage band of 10 to 100 tonnes per annum for the registered substance, and made a testing proposal for an extended one-generation reproductive toxicity study (OECD 443) to be performed with the same analogue substance 3,6-bis(4-tert-butylphenyl)-2,5-dihydropyrrolo[3,4-c]pyrrole-1,4-dione ([redacted]), CAS No 84632-59-7 (EC No 416-250-2). More explicitly, the pup mortality observed in the screening study performed on the analogue substance was considered to constitute an adverse effect that should be further investigated. However, as indicated in section III.1 above, ECHA considers that the read across approach in reference to the reproductive endpoint proposed by the Registrant does not satisfy the requirements of Annex XI section 1.5 and cannot be accepted. Therefore ECHA concludes that the findings of the OECD 421 study on the analogue substance 3,6-bis(4-tert-butylphenyl)-2,5-dihydropyrrolo[3,4-c]pyrrole-1,4-dione ([redacted]), CAS No 84632-59-7 (EC No 416-250-2) – different than for the analogue substance itself – can not be used as a trigger to request a further reproductive toxicity study with the substance subject to the present decision for a registration subject to the requirements of Annex VIII of the REACH Regulation. At this Annex level (for substances registered at 10 to 100 tonnes per annum) the standard information requirement is a screening study on reproduction/developmental toxicity (OECD 421/422).

Therefore, ECHA views that the Registrant did not justify the need for further testing on reproductive toxicity. According to Annex I, the last subparagraph of section 0.5 of the REACH Regulation, if the manufacturer or importer considers that further information is necessary for producing his CSR and that this information can only be obtained by performing tests in accordance with Annex IX and X, he shall submit a proposal for a testing strategy, explaining why he considers that additional information is necessary and record this in the CSR under the appropriate heading.

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 1:

A third party has requested ECHA to direct the Registrant to perform the EOGRTS test, using only one generation.

ECHA notes that the proposed test is rejected.

Third party information 2:

Another third party has indicated that due to the low toxicological activity and that the substance and the structurally related compound of the substance are not absorbed following oral administration and thereof the systemic exposure will not occur, in vivo testing should be prevented based on animal welfare reasons Directive 2010/63/EC).

ECHA notes that the proposed test is rejected.

c) Outcome

Therefore, pursuant to Article 40(3)(d) of the REACH Regulation, the test proposed by the Registrant on the proposed analogue substance 3,6-bis(4-tert-butylphenyl)-2,5-dihydropyrrolo[3,4-c]pyrrole-1,4-dione ([redacted]), CAS No 84632-59-7 (EC No 416-250-2) is rejected since the Registrant has not demonstrated that the requirements of Annex XI section 1.5 for read-across are met. No additional testing is required by ECHA as at the current tonnage level a further reproductive study is not a standard requirement and the Registrant has not justified sufficiently the need for further testing.

IV. 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]
Jukka Malm
Director of Regulatory Affairs