

Decision number: TPE-D-2114312642-60-01/F

Helsinki, 15 January 2016

**DECISION ON TESTING PROPOSAL(S) SET OUT IN A REGISTRATION PURSUANT TO ARTICLE 40(3) OF REGULATION (EC) NO 1907/2006****For 8,9,10,11-tetrachloro-12H-phthaloperin-12-one, CAS No 20749-68-2 (EC No 244-007-9), 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 8,9,10,11-tetrachloro-12H-phthaloperin-12-one, CAS No 20749-68-2 (EC No 244-007-9), submitted by [REDACTED] (Registrant).

- Developmental toxicity / teratogenicity study (OECD 414).

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 16 May 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 the above-mentioned testing proposal for further examination pursuant to Article 40(1) on 15 April 2013.

ECHA held a third party consultation for the testing proposal from 14 August 2014 until 28 September 2014. ECHA received information from third parties (see section III below).

On 10 March 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. That draft decision was based on submission number [REDACTED].

By 17 April 2015 the Registrant did not provide any comments on the draft decision to ECHA.

On 23 July 2015 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. Subsequently, a proposal for amendment to the draft decision were submitted.

On 28 August 2015 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.

The ECHA Secretariat reviewed the proposal for amendment received and amended the draft decision.

On 7 September 2015 ECHA referred the draft decision to the Member State Committee.

By 28 September 2015 the Registrant did not provide any comments on the proposal for amendment.

A unanimous agreement of the Member State Committee on the draft decision was reached on 13 October 2015 in a written procedure launched on 1 October 2015.

ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

## II. Testing required

### A. Tests required pursuant to Article 40(3)

The Registrant shall carry out the following proposed test pursuant to Article 40(3)(a) and 13(4) of the REACH Regulation using the indicated test method and the registered substance subject to the present decision:

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31/OECD 414) in rats or rabbits, oral route.

### 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 **23 January 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 and scientific information submitted by third parties.

### A. Tests required pursuant to Article 40(3)

1. 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.

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 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. ECHA considers these default parameters appropriate and testing should be performed by the oral route with the rat or the rabbit as a first species to be used.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation.

A third party has indicated that "Physicochemical properties of the registered dye, low toxicity in oral acute and sub-acute tests and an assessment of toxicokinetics in the registration dossier suggest that the substance may not be absorbed from the gastrointestinal tract (prediction by Lipinski rule OASIS: not bioavailable). Under these circumstances the proposed test is not expected to add toxicologically meaningful information. In vitro bioavailability studies may provide experimental data on toxicokinetics and help to make an informed decision on the need of the proposed oral prenatal developmental toxicity study."

ECHA notes that it is the Registrant's responsibility to consider and justify in the registration dossier any adaptation of the information requirements in accordance with Annex IX, Section 8.7., column 2, third indent. This adaptation specifies that a pre-natal developmental toxicity study does not need to be conducted if "the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure." ECHA notes that all three criteria need to be met.

ECHA observes that the third party comment addressed only the criterion concerning absorption. However, the third party did not provide in vitro bioavailability studies to prove that no systemic absorption occurs via relevant routes of exposure. Furthermore, an adaptation would also need to demonstrate that the other conditions of the adaptation possibility are fulfilled. Moreover, in this case the substance has a molecular weight of 408 g/mol. Generally, the cut-off level for low absorption is considered 500 g/mol (REACH guidance on information requirements chapter 7c). Physico-chemical parameters do not fully justify the argument of low absorption. In addition, in an oral 28 day repeated dose toxicity study (see ECHA dissemination website), some effects were observed (changes in alkaline phosphatase and histopathology of seminal vesicles), which might point to systemic uptake.

Therefore the criteria listed in Column 2 of Annex IX, section 8.7., third indent are not met and the information requirement for the pre-natal developmental toxicity study cannot be adapted on this basis.

### 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).

#### 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, 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 test, the sample of substance used for the new study 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 test 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 the 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 by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new study 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 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<sup>1</sup> by Ofelia Bercaru, Head of Unit, Evaluation, E3.

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<sup>1</sup> As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.