

Decision number: TPE-D-2114322703-58-01/F

Helsinki, 30 March 2016

DECISION ON TESTING PROPOSAL(S) SET OUT IN A REGISTRATION PURSUANT TO ARTICLE 40(3) OF REGULATION (EC) NO 1907/2006**For 6,15-dihydroanthrazine-5,9,14,18-tetrone, EC No 201-375-5 (CAS No 81-77-6), 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 Articles 10(a)(ix) and 12(1)(d) thereof for 6,15-dihydroanthrazine-5,9,14,18-tetrone, EC No 201-375-5 (CAS No 81-77-6), submitted by [REDACTED] (Registrant).

- Developmental toxicity / teratogenicity study (OECD 414) in rats.

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 4 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.

ECHA received the registration dossier containing the above-mentioned testing proposal for further examination pursuant to Article 40(1) on 2 April 2013.

ECHA held a third party consultation for the testing proposal from 14 August 2014 until 29 September 2014. ECHA received information from third parties (see section III below).

On 28 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 5 October 2015 ECHA received comments from the Registrant agreeing to ECHA's draft decision.

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 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.

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(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 **6 April 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) 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 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 to be performed with the registered substance subject to the present decision (EC No 201-375-5) with the following justification: *"In accordance with Annex IX of EC regulation 1907/2006, the standard information requirement at >100 tpa is a study for developmental toxicity/teratogenicity in one species. The study is generally of low toxicity and the physico-chemical properties indicate that systemic uptake is unlikely. However, in the screening study for reproductive toxicity (OECD 422) one animal showed complete implantation loss at the highest dose level of 1000 mg/kg bw which caused the group average of postimplantation loss to be outside the historical control range. This finding might be incidental, as discussed in detail in the endpoint summary. However, the waiving criteria outlined in column 2 of Annex IX are not fulfilled. Therefore, testing in rats is proposed"*.

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. He did not specify the route for testing. 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. For the reasons explained further below the information provided by third parties is not sufficient to fulfil this information requirement.

A third party has indicated "Low toxicity in acute tests and an oral screening study according to OECD Test Guideline 422 combined with the physicochemical properties suggests that the substance may not be absorbed from the gastro-intestinal 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 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 low toxicity. However, the third party did not 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.

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 [6,15-dihydroanthrazine-5,9,14,18-tetrone]: 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 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 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 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^[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.