EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000004576-67-02/F Helsinki, 22 October 2014

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

For [redacted], CAS No [redacted] (EC No [redacted]), 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) thereof for [redacted] CAS No [redacted] (EC No [redacted]), submitted by [redacted] (Registrant).

- In vivo Mammalian Erythrocyte Micronucleus test (OECD 474)

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 3 January 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 (submission number [redacted]) was confirmed on 2 October 2012.

ECHA held a third party consultation for the testing proposal from 31 January until 18 March 2013 using a more generic public name for the substance (Poly(alkan-2-yl)heteropolycycle). ECHA did not receive information from third parties.

On 13 May, 2013 ECHA sent the draft decision to the Registrant rejecting the testing proposal and invited him to provide comments within 30 days of the receipt of the draft decision. This draft decision was based on submission number [redacted].

On 6 June 2013 ECHA received comments from the Registrant.

The Registrant updated the dossier on 4 June 2013 (submission number [redacted]) and 18 July 2013 (submission number [redacted]) by providing, *in vitro* mammalian chromosome aberration test (OECD 473) results and justification to carry out the test.

The ECHA Secretariat considered the Registrant's comments and update. On the basis of the information, Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

On 3 January 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 proposed test pursuant to Article 40(3)(a) of the REACH Regulation using the indicated test method and the registered substance subject to the present decision:

- Mutagenicity - *In vivo* mammalian erythrocyte micronucleus test (Annex VII, 8.4., column 2; test method B.12./OECD 474).

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **29 April 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.

a) Examination of the testing proposal

An *in vitro* gene mutation study in bacteria is a standard information requirement of column 1 of Annex VII, Section 8.4. of the REACH Regulation. Column 2 of Annex VII, Section 8.4. provides that "Further studies shall be considered in case of a positive result." According to Annex IX, section 8.4, column 2, if there is a positive result in any of the in vitro genotoxicity studies in Annex VII or VIII and there are no results available from an *in vivo* study already, an appropriate *in vivo* somatic cell genotoxicity study shall be proposed by the registrant.

Annex VI, step 4 of the REACH Regulation provides that in some cases, the rules set out in Annexes VII to XI may require certain tests to be undertaken earlier than or in addition to the standard requirements.

The technical dossier contains *in vitro* gene mutation studies in bacteria and in mammalian cells with negative results and an *in vitro* chromosomal aberration study in mammalian cells

with a positive result. The positive result indicates that the substance is inducing chromosomal aberrations under the conditions of the test.

An appropriate *in vivo* genotoxicity study to follow up the concern on chromosomal aberrations is not available for the registered substance. The Registrant considers it necessary to provide further information for this endpoint and has submitted a testing proposal for an *in vivo* mammalian erythrocyte micronucleus test in rats according to test method OECD 474. The Registrant justifies the suggested test, as follows: '*Since the in vitro chromosome aberration test was positive, the substances might have a clastogenic potential. According to the REACH regulation, "appropriate in vivo mutagenicity studies shall be considered in case of a positive result in any of the genotoxicity studies in Annex VII or VIII". A micronucleus assay according to OECD TG 474 is such an appropriate study from our perspective. Furthermore, especially in case of the required reproductive toxicity screening test according to section 8.7.1 of Annex VIII it is important to clarify potential genotoxic properties before conducting the test. In case genotoxic properties are confirmed this test might not be necessary. In section 7.6.2 of this dossier we therefore propose to conduct an in vivo micronucleus assay.*'

ECHA considers that the Registrant has adequately shown the need to do the above test, which, in ECHA's view, is an appropriate test to investigate effects on chromosomal aberrations *in vivo* as described in the ECHA Guidance document on information requirements and chemical safety assessment, chapter R.7.7.1. and figure R.7.7-1 (August 2013).

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study with the registered substance subject to the present decision: *In vivo* mammalian erythrocyte micronucleus test (test method: EU B.12./OECD 474).

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. 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.

[redacted]
Leena Ylä-Mononen
Director of Evaluation