EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000001958-60-05/F Helsinki, 9 March 2012

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

For 2,2'-dimethyl-2,2'-azodipropiononitrile, CAS No 78-67-1 (EC No 201-132-3), 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 proposals submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12(1)(e) thereof for **2,2'-dimethyl-2,2'-azodipropiononitrile**, CAS No 78-67-1 (EC No 201-132-3), by [redacted] (Registrant), latest submission number [redacted], for the tonnage band of 1000 tonnes or more per year:

1. Repeated Dose 90-day Oral toxicity in Rodents (OECD 408), rat, oral route, Annex IX, 8.6.2;
2. Pre-natal Developmental Toxicity Study (OECD 414), rat, Annex IX, 8.7.2;
3. Aerobic Mineralisation in Surface Water – Simulation Biodegradation Test (OECD 309); and
4. Two-Generation Reproduction Toxicity Study (OECD 416), rat, Annex X, 8.7.3.

The present decision relates solely to the examination of the testing proposal for a sub-chronic toxicity study (90-day), pre-natal developmental toxicity study and simulation testing on ultimate degradation in surface water. The testing proposal for the two-generation reproductive toxicity study is addressed in a separate decision although all testing proposals were initially addressed together in the same draft decision.

On 8 October 2010, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of the testing proposals set out by the Registrant in the registration dossier for the substance mentioned above.

ECHA held a third party consultation for the testing proposals from 15 March 2011 until 29 April 2011. ECHA did receive information from third parties (see section III below).

On 14 September 2011 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 15 October 2011 the Registrant did not provide any comments on the draft decision to ECHA.

On 4 November 2011 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, Competent Authorities of the Member States submitted proposals for amendment to the draft decision.

On 8 December 2011 ECHA notified the Registrant of proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on those proposals for amendment within 30 days of the receipt of the notification.

ECHA reviewed the proposals for amendment received and decided to amend the draft decision.

On 19 December 2011 ECHA referred the draft decision to the Member State Committee.

On 6 January 2012 the Registrant provided comments on the proposed amendments. The Member State Committee took the comments of the Registrant into account.

After discussion in the Member State Committee meeting on 6-10 February 2012, the draft decision was split into two draft decision documents, one relating to the testing proposal for a two-generation reproductive toxicity study and one relating to the testing proposals for sub-chronic toxicity study (90-day), pre-natal developmental toxicity study and simulation testing on ultimate degradation in surface water.

Regarding the draft decision on the repeated-dose 90-day toxicity study, pre-natal developmental toxicity study and simulation testing on ultimate degradation in surface water, the Member State Committee further modified the draft decision and a unanimous agreement of the Committee was reached on 8 February 2012.

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 to initiate a compliance check on the present dossier at a later stage.

II. Testing required

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

1. Sub-chronic toxicity study (90-day) in rats, oral route (Annex IX, 8.6.2.; test method: EU B.26/OECD 408).
2. Pre-natal developmental toxicity study in rats, oral route (Annex IX, 8.7.2.; test method: EU B.31/OECD 414).
3. Simulation testing on ultimate degradation in surface water (Annex IX, 9.2.1.2.; test method: EU C.25/OECD 309)

The Registrant shall determine the appropriate order of the studies taking into account the possible outcome and considering the possibilities for adaptations of the standard information requirements according to column 1 or 2 provisions of the relevant Annexes of the REACH Regulation.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **9 March 2013** from the date of the decision an update of the registration dossier containing the information required by this decision.

Data from a second pre-natal developmental toxicity study on another species is a standard information requirement according to Annex X, 8.7.2. of the REACH Regulation, subject to the Annex IX, 8.7.2. column 2 requirements. If the Registrant considers that testing is necessary to fulfil this information requirement taking into account the outcome of the pre-natal developmental toxicity study on a first species and all other relevant and available data, he should include in the update of his dossier a testing proposal for a pre-natal developmental toxicity study on a second species.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposals of the Registrant for the registered substance and scientific information submitted by third parties. The performance of these studies is subject to all appropriate column 2 or Annex XI data adaptations.

1. Sub-chronic toxicity study (90-day)

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation ECHA may take a decision requiring the Registrant to carry out the proposed test and setting a deadline for the submission of the requested information.

A sub-chronic toxicity study (90-day) is required under Annex IX, 8.6.2. Since information on this endpoint is missing or inadequate in the registration dossier, and since no acceptable adaptations to omit these information requirements have been received from either the Registrant or third parties (see below), ECHA decided to accept the proposed test.

b) Consideration of the information received during third party consultation

The third party information following the public consultation was evaluated in order to determine whether there is already scientifically valid information that addresses the relevant substance and hazard endpoint. This additional information does not, however, change the conclusion that a sub-chronic toxicity need to be requested, as explained below.

A third party has proposed the following information for ECHA to consider, i.e. the use of read-across from an existing combined study on repeated dose toxicity with reproduction/developmental screening test performed with another substance than the registered substance and the use of the Threshold of Toxicological Concern (TTC) concept before a sub-chronic toxicity study is carried out.

ECHA notes that the sub-chronic toxicity study is a standard information requirement according to Annexes IX, 8.6.2. of the REACH Regulation. Considering that ECHA invited submission of "scientifically valid information and studies that address the relevant substance and hazard end-point, addressed by the testing proposal", as specified by Article 40(2), ECHA has evaluated the information provided by the third party. ECHA has concluded that the proposed information does not sufficiently address the relevant endpoint. Consequently, ECHA concludes that the information provided is not a basis for rejecting the testing proposed.

c) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Sub-chronic toxicity study (90-day) (Annex IX, 8.6.2, method B.26 of Regulation (EC) No 440/2008, OECD test guideline 408) in rat by the oral route.

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.

2. Pre-natal developmental toxicity study

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation ECHA may take a decision requiring the Registrant to carry out the proposed test and setting a deadline for the submission of the requested information.

A pre-natal developmental toxicity study is required under Annex IX, 8.7.2. Since information on this endpoint is missing or inadequate in the registration dossier, and since no acceptable adaptations to omit these information requirements have been received from either the Registrant or third parties (see below), ECHA decided to accept the proposed test.

b) Consideration of the information received during third party consultation

The third party information following the public consultation was evaluated in order to determine whether there is already scientifically valid information that addresses the relevant substance and hazard endpoint. This additional information does not, however, change the conclusion that a pre-natal developmental toxicity study needs to be requested, as explained below.

A third party has proposed the use of read-across from an existing combined study on repeated dose toxicity with reproduction/developmental screening test performed with another substance than the registered substance, an *in vitro* test and QSAR models, and an extended one generation reproductive toxicity test to waive the developmental toxicity study.

ECHA notes that the pre-natal developmental toxicity study is a standard information requirement according to Annexes IX and X, 8.7.2. of the REACH Regulation. Considering that ECHA invited submission of "scientifically valid information and studies that address the relevant substance and hazard end-point, addressed by the testing proposal", as specified by Article 40(2), ECHA has evaluated the information provided by the third party. The information provided by the third party does not meet the specific rules for adaptation of the information requirement for pre-natal developmental toxicity studies under column 2 of Annexes IX and X, 8.7. Specifically it was not proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure. The OECD test guideline for an extended one generation reproductive toxicity study (EOGRTS, OECD TG 443) has been adopted by the OECD Council on 28 July 2011. Although not yet adopted for the EU Test Method Regulation, the TG 443 is now an internationally accepted test method and according to Article 13(3) of the REACH Regulation it can in principle be applied to generate information on intrinsic properties subject to being recognised as appropriate by the Commission or the Agency. In EOGRTS the developmental toxicity parameters such

as skeletal and visceral malformations are not examined and, thus, EOGRTS does not provide adequate information on developmental toxicity to waive the prenatal developmental toxicity study. Therefore, the third party proposal does not provide a sufficient basis on which to reject the proposed tests.

c) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Pre-natal developmental toxicity study (Annex IX, 8.7.2, method B.31 of Regulation (EC) No 440/2008, OECD test guideline 414) in rat by the oral route.

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.

3. Simulation testing on ultimate degradation in surface water

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation ECHA may take a decision requiring the Registrant to carry out the proposed test and setting a deadline for the submission of the requested information.

According to column 1, Section 9.2.1.2 of Annex IX of the REACH Regulation, simulation testing on ultimate degradation in surface water is required to fulfil the standard information requirements. Column 2 of Section 9.2 of Annex IX further indicates that this information requirement must be fulfilled unless the chemical safety assessment leads to the conclusion that the test is not needed.

The Registrant has submitted a testing proposal for a simulation biodegradation study in surface water to cover this endpoint and has provided no adaptation of the standard information requirements according to column 2. The Registrant has based their proposal on the results from a screening test for biodegradability, which indicated minimal biodegradation, and on the data on environmental distribution reported in the registration dossier.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Simulation testing on ultimate degradation in surface water (Annex IX, 9.2.1.2, method C.25 of Regulation (EC) No 761/2009, OECD Guideline 309).

4. Deadline for submitting the information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 36 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also requested a 2-generation reproductive toxicity study. As the testing proposal for this study is not addressed in the present draft decision, ECHA considers that a reasonable time period for providing the required information in the form of an updated IUCLID5 dossier is 24 months from the date of the adoption of the decision. The decision was therefore modified accordingly.

IV. General requirements for the generation of information and Good Laboratory Practice

ECHA always 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). National authorities monitoring GLP maintain lists of test facilities indicating the relevant areas of expertise of each facility.

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.

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://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.

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