EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002477-69-03/F Helsinki, 15 May 2013

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

For Reaction products of 2-(4,6-bis(2,4-dimethylphenyl)-1,3,5-triazin-2-yl)-5-hydroxyphenol with ((C10-16, rich in C12-13 alkyloxy)methyl)oxyrane , EC No 410-560-1, 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)(d) thereof for Reaction products of 2-(4,6-bis(2,4-dimethylphenyl)-1,3,5-triazin-2-yl)-5-hydroxyphenol with ((C10-16, rich in C12-13 alkyloxy)methyl)oxyrane, EC No 410-560-1, by [redacted] (Registrant), latest submission number [redacted], for the tonnage band of 100 to 1000 tonnes per year. This decision does not take into account any updates after 18 January 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.

- *Daphnia magna* Reproduction Test (OECD 211);
- Earthworm, Acute Toxicity Tests (OECD 207);
- Two-generation Reproduction Toxicity Study (OECD 416); and
- Prenatal Developmental Toxicity Study (OECD 414).

The examination of the testing proposals was initiated upon the date when receipt of the complete registration dossier was confirmed on 17 November 2011.

ECHA held a third party consultation for the testing proposals from 16 January 2012 until 01 March 2012. ECHA did receive information from third parties (see section III below).

On 15 May 2012 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 1 June 2012 ECHA received comments from the Registrant.

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

On 18 January 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, the Competent Authorities of the Member States did not propose amendments to the draft decision and ECHA took the decision pursuant to Article 51(3) 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 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. Long-term toxicity testing on aquatic invertebrates (Annex IX, 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211); and
2. Pre-natal developmental toxicity study in rats or rabbits, oral route (Annex IX, 8.7.2.; test method: EU B.31/OECD 414); and
3. Short-term toxicity to terrestrial invertebrates (Annex IX, 9.4.1.; test method: Toxicity for earthworms, EU C.8/OECD 207);
   or
   Long-term toxicity on terrestrial invertebrates (Annex IX, 9.4. column 2; test method: Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*), OECD 222; or Enchytraeid reproduction test, OECD 220; or Collembolan reproduction test in soil, OECD 232).

while the originally proposed test for a Two-generation Reproduction Toxicity Study (OECD 416) proposed to be carried out using the registered substance is rejected pursuant to Article 40(3)(d) of the REACH Regulation.

The Registrant shall determine the appropriate order of the studies taking into account the possible outcomes 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.

Once results of the proposed test on long-term toxicity to aquatic invertebrates are available, the Registrant shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation. If the revised chemical safety assessment indicates the need to investigate further the effects on aquatic organisms, the Registrant shall consider submitting a testing proposal for a long-term toxicity test on fish in order to fulfil the standard information requirement of Annex IX, 9.1.6.

Once results of the requested toxicity test on terrestrial invertebrates are available, the Registrant shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation. He shall furthermore consider whether there is a need to investigate further the effects on terrestrial organisms in order to fulfil the standard information requirements of Annex IX, 9.4. If the Registrant concludes that further investigation of effects on terrestrial organisms is required, he shall submit testing proposals for additional toxicity tests. If the Registrant concludes that no further investigation of effects on

terrestrial organisms is required, he shall update his technical dossier by clearly stating the reasons for adapting the standard information requirements of Annex IX, 9.4.2 and 9.4.3. of the REACH Regulation.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **15 February 2015** an update of the registration dossier containing the information required by this decision.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposals submitted by the Registrant for the registered substance.

1. Long-term toxicity testing on aquatic invertebrates

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

Long-term toxicity testing on invertebrates is a standard information requirement as laid down in Annex IX, 9.1.5. of the REACH Regulation. Column 2 of Section 9.1. 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 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.

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 1.1., August 2008), Chapter R7b, Figure R.7.8-4 page 53, if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. According to the integrated testing strategy, the Daphnia study is to be conducted first. If based on the results of the long-term Daphnia study and an applied assessment factor of 50 no risks are indicated, no long-term fish testing may need to be conducted.

Therefore, pursuant to Article 40(3)(a)of the REACH Regulation, the Registrant is required to carry out the proposed study: Long-term toxicity testing on aquatic invertebrates (Annex IX, 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211) using the registered substance.

2. Pre-natal developmental toxicity study

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 did not specify the species and route to be used 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.

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 in rats or rabbits, oral route (Annex IX, 8.7.2.; test method: EU B.31/OECD 414) using the registered substance.

3. Effects on terrestrial organisms (Section II, test 3)

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

In order to fulfil the standard information requirements set out in Annex IX, section 9.4., the Registrant should provide the following studies: (i) short term toxicity to invertebrates (section 9.4.1.), (ii) effects on soil micro-organisms (section 9.4.2.) and (iii) short term toxicity to plants (section 9.4.3.). Column 2 of Annex IX, section 9.4. advises the Registrant to consider long term toxicity testing instead of short term in particular for substances that have a high potential to adsorb to soil or that are very persistent.

In the registration dossier, the Registrant has proposed an earthworm acute toxicity test according to OECD 207 in order to fulfil all three standard information requirements in section 9.4. of Annex IX of the REACH Regulation.

It is noted that the proposed test only addresses invertebrates (i.e. the information requirement in Annex IX, section 9.4.1.) and does not address the other two trophic levels requested for this tonnage band (i.e. the information requirements in Annex IX, sections 9.4.2. and 9.4.3.). The test proposed by the Registrant in the registration dossier may therefore not be sufficient, on its own accord, to fulfil all the information requirements outlined in Annex IX, 9.4., since it does not fulfil the information requirements laid down in Annex IX, sections 9.4.2. and 9.4.3. Accordingly, ECHA included these studies in the draft decision sent to the Registrant for comments.

In his comments on the draft decision, the Registrant elaborated on the justifications in the registration dossier for waiving of studies on the effects on soil micro-organisms (Annex IX, section 9.4.2.) and short term toxicity to plants (Annex IX, section 9.4.3.) in accordance with the specific rules for adaptation indicated in column 2 of Annex IX. More specifically the Registrant reflected on the substance properties (water solubility, log Koc) and concluded that the substance will be bound to the soil phase and that exposure via pore water will be less relevant. The Registrant also highlighted the absence of toxicity of the registered substance in standard acute toxicity tests. The draft decision was therefore amended and the requirements for these tests were removed.

The Registrant originally proposed to undertake a short term toxicity test to earthworms (OECD 207). However, based on the substance properties ECHA considers a long term toxicity test to be more appropriate. In his comments on the draft decision, the Registrant acknowledged that long term testing would be more appropriate given the substance properties and agreed to perform a long-term toxicity test on terrestrial invertebrates according to OECD 222 by stating the following "*we will conduct a long-term toxicity test to terrestrial invertebrates (OECD 222) which is the appropriate test due to the substance*

properties". The draft decision was not amended in this regard, however ECHA supports the Registrant's decision to proceed with long term testing.

Therefore, pursuant to Article 40(3)(a) ECHA has accepted the Registrant's testing proposal and the Registrant is required to perform a long term toxicity to terrestrial invertebrates (Annex IX, 9.4., column 2, OECD 222 or OECD 220 or OECD 232) or a short term toxicity to terrestrial invertebrates (Annex IX, 9.4.1., OECD 207) test.

The Registrant shall determine the need to submit testing proposals for further terrestrial toxicity tests based on the outcome of the OECD 222 OECD 220, OECD 232 or OECD 207 test and the considerations set out in Table R.7.11.-2 of Guidance R7.C if applicable.

The assignment of the registered substance to a soil hazard category, as laid out in ECHA guidance section R.7.11.6, may become relevant following completion of the *Daphnia magna* reproduction test. Therefore it is advisable that the *Daphnia magna* reproduction test be performed first and the impact of the results of both this and, if appropriate, other required tests on the CSA evaluated before proceeding with the required terrestrial toxicity test.

4. Two-generation Reproduction Toxicity Study

a) Examination of the testing proposal

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

A two generation reproductive toxicity study is required at this tonnage level if the 28-day or 90-day study indicates adverse effects on reproductive organs or tissues (Annex IX, 8.7.3.).

Currently there is no information available in the dossier which indicates that the conditions for requiring a two-generation reproductive toxicity study are fulfilled. The Registrant has included a 28-day study in the registration dossier which shows no such adverse effects on the reproductive organs or tissues. Additionally, the Registrant has chosen to adapt the standard information requirement of Annex IX, 8.6.2 of the REACH regulation for sub-chronic toxicity (90-day) stating that "*the substance did not cause adverse or irreversible effects in the course of the 28d study. Thus, it is not likely that prolonged in-depth examination of the observed effects (90d study) reveals an escalation of the known symptoms leading to a classification. Moreover, a 2-Generation study according OECD guideline 416 is proposed which provides additional experimental data of the P and F1 generation (clinical observations, data on body weight development and food/water comsumption, gross necropsy and organ weights, histopathology of identified target organs or gross leasions) to derive information on bioavailability and systemic effects after subchronic (> 10 weeks) dose administration*". ECHA therefore concludes that at this moment in time the legal requirements of Annex IX for the mandatory performance of the two-generation study are not met since no adverse effects on reproductive organs or tissues were observed in the available 28-day study and no 90-day study is available at present.

If based on the outcome of the present decision the Registrant considers the adaptation provided for the 90-day study as no longer appropriate and deems testing necessary to fulfil the information requirement of Annex IX, 8.6.2 of the REACH regulation he should include in the update of his dossier a testing proposal for a sub-chronic toxicity study (90-day).

If the results of a sub-chronic toxicity study (90-day) indicate adverse effects on reproductive organs or tissues then the Registrant shall submit a testing proposal to cover the endpoint of Annex IX, 8.7.3. for reproductive toxicity unless the Registrant considers that the specific rules for adaptation from this information requirement mentioned in Column 2, Annex IX, 8.7 apply.

In any event the Registrant may on the basis of other considerations submit a testing proposal to cover the Annex IX, 8.7.3. endpoint for reproductive toxicity at an earlier stage. Appropriate reasons for testing should in that instance be provided.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation concerning an alternative study to the two-generation reproduction toxicity study proposed by the Registrant. For the reasons explained above the testing proposal is rejected and consequently the information provided by third parties was not considered further.

c) Outcome

The testing proposal is currently rejected. If a 28-day or 90-day study shows adverse effects on reproductive organs or tissues, the Registrant shall submit a testing proposal to cover the endpoint of Annex IX, 8.7.3. as this would then constitute a standard information requirement for substances registered at 100 to 1000 tonnes per year.

In any event the Registrant may on the basis of other considerations submit a testing proposal to cover the Annex IX, 8.7.3. endpoint for reproductive toxicity at an earlier stage. Appropriate reasons for testing should in that instance be provided.

IV. Adequate identification of the composition of the tested material

The process of evaluation of testing proposals set out in Article 40 of the REACH Regulation aims at ensuring that the new studies 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 evaluation of the testing proposal. The Registrant must note, however, that this information has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In addition, it is important to ensure that the particular sample of substance tested in the new studies 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. If the registration of the substance covers different grades, the sample used for the new studies must be suitable to assess these.

Finally, there must be adequate information on substance identity for the sample tested and the grade registered to enable the relevance of the studies 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://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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