EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002528-70-06/F Helsinki, 20 December 2012

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

For Phosphonium, tetrakis(hydroxymethyl)-, chloride (1:1), reaction products with 1-tetradecanamine and urea, CAS No 359406-89-6 (EC No 436-230-7), 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 Phosphonium, tetrakis(hydroxymethyl)-, chloride (1:1), reaction products with 1-tetradecanamine and urea, CAS No 359406-89-6 (EC No 436-230-7), by [redacted] (Registrant).

- 90-day oral toxicity study (OECD 408) in rodents, oral route using the analogue substance tetrakis(hydroxymethyl) phosphonium chloride, oligomeric reaction products with urea (CAS No 27104-30-9, EC No 500-057-6), additionally comprising (i) recovery groups to evaluate the reversibility of liver effects, and (ii) specific assessment of effects on the reproductive cycle.

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 19 July 2012, 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 was confirmed on 20 December 2011.

ECHA held a third party consultation for the testing proposal from 6 March 2012 until 20 April 2012. ECHA did not receive information from third parties.

On 8 June 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.

By 9 July 2012 the Registrant did not provide any comments on the draft decision to ECHA.

On 19 July 2012 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, one Competent Authority of a Member State submitted a proposal for amendment to the draft decision.

On 22 August 2012 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.

ECHA has reviewed the proposal for amendment received and decided to amend the draft decision accordingly.

On 3 September 2012 ECHA referred the draft decision to the Member State Committee.

On 5 September 2012, the Registrant provided comments on the proposed amendment. The Member State Committee took the comments of the Registrant into account.

A unanimous agreement of the Member State Committee on the draft decision was reached on 8 October 2012 in a written procedure launched on 26 September 2012 and ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Testing required

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

> Sub-chronic toxicity study (90-day) in rats, oral route (Annex IX, 8.6.2.; test method: EU B.26/OECD 408) using the registered substance.

while the originally proposed test for a 90-day oral toxicity study (test method: EU B.26/OECD 408) proposed to be carried out using the analogue substance tetrakis(hydroxymethyl) phosphonium chloride, oligomeric reaction products with urea is rejected pursuant to Article 40(3)(d) of the REACH Regulation.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **20 June 2014** 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 proposal submitted by the Registrant for the registered substance.

a) Examination of the testing proposal

Pursuant to Article 40(3)(d) and 40(3)(c) of the REACH Regulation, ECHA may reject the proposed test and require the Registrant to carry out other tests in case of non-compliance of the testing proposal with Annexes IX, X or XI of the REACH Regulation.

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, section 8.6.2. 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 column 2 adaptation according to Annex IX, Section 8.6.2 of the REACH Regulation might apply; however, the Registrant included a testing proposal for a sub-chronic toxicity study (90 day) to scientifically investigate whether (i) the liver is the target organ and (ii) the observed effects are reversible (cf. Chemical Safety Report as filed with the updated dossier, page 40).

ECHA observes that in the testing proposal the Registrant has proposed to use the analogue substance tetrakis(hydroxymethyl) phosphonium chloride, oligomeric reaction products with urea (CAS No 27104-30-9, EC No 500-057-6) as test material instead of the registered substance; hence, the proposed study includes a read-across approach from the analogue substance (i.e. the source substance) to the registered substance.

The Registrant has justified the read-across approach as follows (cf. section 7.5.1 of the corresponding IUCLID dossier):

> "It is considered appropriate to read across data [...] because the substances have similar chemical structures. The acute studies and 28-day repeat dose oral toxicity studies for the two substances demonstrate that their toxicological profile is similar. For both substances, liver toxicity is the critical effect for risk assessment, with effects at equivalent dose levels in the 28-day study being almost identical. A single study is considered sufficient to provide the data necessary for risk assessment for both substances and is in line with the aim of minimising vertebrate testing on the grounds of animal welfare."

If the Registrant proposes to carry out the tests required by Annex IX with a substance other than the registered substance, Article 13(1) and Annex IX, third introductory paragraph, require the Registrant to clearly state reasons for adapting the standard information according to the rules in Annex XI.

Annex XI, Section 1.5. governing the "grouping of substances and read-across approach" provides that substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as a group, or 'category' of substances. Application of the group approach requires that physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s) by interpolation to other substances in the group (read-across approach). It is further required by Annex XI, Section 1.5. that "adequate and reliable documentation of the applied method shall be provided."

In the present case, ECHA notes that the Registrant has failed to explain how the similarities in composition and the information in the dossier on the physicochemical properties would allow for the prediction of the endpoint under consideration for the registered substance.

Furthermore, ECHA notes that in the registration dossier submitted by the Registrant, adequate and reliable evidence that the source substance and the registered substance exhibit similar toxicological properties are missing. The Registrant has merely stated that certain toxicological properties are similar without giving further evidence. In particular,

ECHA notes that "adequate and reliable documentation of the applied method" in the form of a scientificly credible explanation as to how the prediction can be made is lacking in the dossier.

Moreover, it should be emphasised that the registered substance comprises THPC, urea and C_{14}-amine, whereas the source substance only comprises THPC and urea. The source substance does not comprise an organic amine, let alone C_{14}-amine. In this respect, it should be noted that the Registrant has provided no adequate and reliable justification as to why the absence of C_{14}-amine in the source substance is acceptable for the read-across approach for the specific toxicological endpoint.

On the basis of the above, ECHA concludes that as adequate justification for the proposed read-across is not provided with respect to the chemical-similarity requirement according to Annex XI, Section 1.5. of the REACH Regulation, the read-across proposal cannot be accepted.

As part of the EU B.26 (OECD 408) guideline, the Registrant has proposed to include
(i) recovery groups to evaluate the reversibility of liver effects, and
(ii) specific assessment of effects on the reproductive cycle.

According to section 1.5.2 of EU Method B.26, animals in a satellite group scheduled for follow-up observations to detect persistence of, or recovery from toxic effects may be included in the 90-day study. Furthermore, the method places additional emphasis on reproductive effects and should allow for the identification of chemicals with the potential to cause reproductive organ effects, which may warrant further indepth investigation (cf. section 1.1 of EU Method B.26). Therefore, ECHA considers that the additional measurements proposed by the Registrant to investigate (i) the reversibility of liver effects and (ii) effects on the reproductive cycle are consistent with EU Method B.26 and may be included in the 90-day study.

ECHA notes that it is at the Registrant's discretion to perform the additional examinations as part of the repeated dose toxicity study and use the results to ensure the safe use of the substance. However, the Registrant is reminded that the proposed extension of this study will not fulfil the standard information requirement for reproductive toxicity according to Annex VIII and Annex IX, Section 8.7, unless adaptation according to column 2 of the respective Annexes is applicable.

With regard to the selection of the appropriate route of administration, the Registrant has proposed testing by the oral route. In the light of the physico-chemical properties of the substance and the information provided on the uses and human exposure, ECHA considers that testing by the oral route is appropriate.

The Registrant has not specified the species to be tested. According to the test method EU B.26/OECD 408 the rat is the preferred rodent species. ECHA considers this species as being appropriate.

b) Outcome

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is required to carry out the following study: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD 408) using the registered substance. The originally proposed test for a 90 day oral toxicity study the analogue substance [Phosphonium, tetrakis(hydroxymethyl)-, chloride (1:1), reaction products with 1-tetradecanamine and urea] is rejected in accordance with Article 40(3)(d).

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.

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 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 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 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. If the registration of the substance covers different grades, the sample used for the new study must be suitable to assess these.

Furthermore, there must be adequate information on substance identity for the sample tested and the grade 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://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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