ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002616-73-05/F Helsinki, 22 July 2013

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

**For Trichloroacetic acid, CAS No 76-03-9 (EC No 200-927-2), 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)(e) thereof for trichloroacetic acid, CAS No 76-03-9 (EC No 200-927-2), by [redacted] (Registrant):

- Developmental toxicity / teratogenicity study (OECD 414) with the substance sodium chloroacetate to confirm effects on spermatogenesis observed in a 90-day toxicity study in the dog with the substance sodium trichloroacetate.

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 8 March 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.

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.

On 23 September 2010, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of the testing proposal set out by the Registrant in the registration dossier for the substance mentioned above.

ECHA held third party consultations for the testing proposal: first for Reproductive toxicity (two-generation reproductive toxicity) from 16 June 2011 until 1 August 2011 and then for Reproductive toxicity (pre-natal developmental toxicity) from 14 October 2011 until 28 November 2011. ECHA did receive information from third parties (see section III below).

On 16 November 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 17 December 2012 ECHA received comments from the Registrant agreeing to ECHA's draft decision.

ECHA considered the Registrant's comments received. The comments are reflected in the Statement of Reasons (Section III) whereas no amendments to the Testing Required (Section II) were made.

On March 8 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, Competent Authorities of the Member States submitted proposals for amendment to the draft decision.

On 11 April 2013 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 22 April 2013 ECHA referred the draft decision to the Member State Committee.

On 13 May 2013 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 11-14 June 2013, a unanimous agreement of the Member State Committee on the draft decision as modified at the meeting was reached on 13 June 2013. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

## II. Testing required

The Registrant shall carry out the following test pursuant to Article 40(3)(b) of the REACH Regulation using the indicated test methods and the sodium salt of the registered substance:

- Pre-natal developmental toxicity study in rabbits, oral route (Annex IX, 8.7.2.; test method: EU B.31/OECD 414);

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **22 July 2014** 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 and scientific information submitted by third parties.

In relation to the testing proposal subject to the present decision, the Registrant had initially proposed to use a read-across and grouping approach, in accordance with Annex XI, 1.5, and conduct a developmental toxicity study according to OECD guideline 414 on an analogue substance sodium monochloroacetate and to use the results to address the endpoint requirements for pre-natal developmental toxicity and two-generation reproductive toxicity for the substance subject to this decision.

ECHA found incompatibilities in the proposed read-across and grouping strategy, notably on different toxicities of the substances and the number of chlorine atoms in the different substances which were not addressed in the category hypothesis or category justification provided by the Registrant. Based on this, ECHA concluded in the Draft Decision notified to the Registrant that the criteria of Annex XI 1.5 of the REACH Regulation were not fulfilled.

The Registrant stated in their comments that they agree with ECHA that read across to the proposed analogue substance is invalid.

After receiving the Draft Decision the Registrant has updated the technical dossier of the originally proposed analogue substance sodium monochloroacetate. In that dossier, the Registrant replaced the initial testing proposal for reproductive toxicity with exposure based waiving adaptation. The technical dossier of the substance subject to this decision has not been updated.

a) Examination of the testing proposal

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

Pre-natal developmental toxicity studies are part of the standard information requirements as laid down in Annex IX, section 8.7.2. of the REACH Regulation. Annex IX, section 8.7.2., column 2 provides that the decision on the need to perform a pre-natal developmental toxicity study at a tonnage level of 100 to 1000 tonnes per annum or 1000 tonnes per annum or more on a second species should be based on the outcome of the first test and all other relevant and available data.

In the dossier on the substance subject to the present decision, the Registrant reported a key study "equivalent or similar" to OECD Guideline 414 (Prenatal Developmental Toxicity Study) on rats with the registered substance trichloroacetic acid and concluded that the substance was considered to be developmentally toxic. However, the Registrant did not self-classify the registered substance to Repr 1B:H360D.

Under the heading "Toxicity for reproduction", section 7.8 (summary) and in the end point study record 7.8.1 in the IUCLID file of the technical dossier, the Registrant included a testing proposal for a study to be conducted according to OECD Guideline 414 (Prenatal Developmental Toxicity Study). The testing proposal originally referred to the use of the analogue substance sodium monochloroacetate to fulfil the information requirement. However, after receiving the initial Draft Decision where ECHA indicated that the proposed read across and grouping strategy is not adequately justified to cover the information requirements of the substance subject to this decision, the Registrant concluded in their comments that they do not have an objection regarding the decision on testing this endpoint.

ECHA has examined this testing proposal considering all the relevant and available data in the technical dossier and the information submitted by third parties during the public consultation. Although the Registrant concludes that the substance is a developmental toxicant, he has not proposed self-classification as toxic for Reproduction category 1B but made a testing proposal to further characterise the developmental toxicity. In accordance with the provisions of Annex IX, section 8.7.2., column 2 of the REACH Regulation it is necessary to provide additional information for this endpoint by providing information on a pre-natal developmental toxicity study in a second species with the substance subject to the present decision.

The registered substance needs to be buffered, to avoid the potential for effects due to the corrosive properties, before administration. Under physiological conditions, trichloroacetic acid dissociates to the respective trichloroacetate ion and the salts are therefore expected to be toxicologically equivalent to the respective free acid, except for the corrosive properties of strong solutions of the acid. Therefore, ECHA requires the Registrant to use the sodium salt of trichloroacetic acid for testing for reproductive toxicity instead of the free acid.

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 rabbit as a second species to be used.

ECHA would like to remind the Registrant that the study does not need to be conducted if the substance is known to cause developmental toxicity meeting the criteria for classification as Toxic for Reproduction Category 1A or 1B reproductive toxicant: H360D (according to Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures) and the available data are adequate to support a robust risk assessment.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal (pre-natal developmental toxicity) 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.

Third party information 1:

A third party has submitted a comment that - based on the uses registered in the joint submission dossier for monochloroacetic acid (MCAA) and sodium monochloroacetate (SMCA) "a pre-natal developmental toxicity study is not necessary ("exposure-based waiving", REACH Annex XI)". The third party further commented that from a scientific perspective based on available data, read-across for systemic effects is justified from SMCA to MCAA or vice-versa due to monochloroacetate moiety or from sodium trichloroacetate (STCA) to trichloroacetic acid (TCAA) or vice-versa due to trichloroacetate moiety, but not from MCAA or SMCA to TCAA or STCA (or vice-versa). To support this conclusion, the third party provided a table "human toxicity endpoint comparisons" that contains data on MCAA and TCAA from REACH dossiers "as published on ECHA-Chem".

Regarding exposure-based waiving, it is at the Registrant's discretion to consider possible adaptations. However, the information on exposure given in the registration dossier is not sufficient to use this adaptation.

ECHA acknowledges the information provided by the third party on application of read-across between TCAA/STCA. ECHA agrees to the extent that the trichloroacetic acid and its respective sodium salt can be regarded as toxicologically equivalent except for the corrosive properties of the respective acid.

Third party information 2:

A third party has submitted a comment "on studies which are not yet summarized in the registration dossiers, for a risk assessment as a chemicals category favoured by the registrants."

Within their comment, the third party summarised that "A category approach of chlorinated acetic acids can also rely on two published studies with dichloroacetic acid which have not yet been included in the dossiers. This would result in a presumably conservative risk assessment and classification of chloroacetic acid and sodium chloroacetate as developmental toxicants." Third party also concluded that "exposure and risk reduction strategy of registrants cited in the EU Risk Assessment Report should also have to be taken into consideration when evaluating the need of a prenatal developmental toxicity study of sodium monochloroacetate." In addition the comment included information and links to existing data for pre-natal developmental toxicity of mono-, di- and trichloroacetic acid and previous assessment of human health risks of chloroacetic acid and sodium chloroacetate for risk assessment as a chemical category favoured by the Registrant.

ECHA acknowledges the information provided by the third party but notes that the information they provide is not itself sufficient to fulfil the information requirement for pre-natal developmental toxicity for the registered substance. The additional references provided by the third party do not fulfil the read-across requirements stated in Annex XI 1.5 fulfilled. However, the Registrant may wish to take note of the additional information that exists on dichlorinated species.

ECHA concludes that the EU risk assessment report and related documents do not provide information that could be used to cover information requirements for the developmental toxicity of trichloroacetic acid.

Regarding the 3rd party information on "exposure and risk reduction strategy" it is at the Registrant's discretion to consider possible adaptations. However, the information on exposure given in the registration dossier is not sufficient for the use of exposure-based adaptation.

c) Outcome

ECHA has examined this testing proposal considering all the relevant and available data in the technical dossier and the information submitted by third parties during the public consultation. The available information is not considered as sufficient to permit a robust conclusion on the developmental toxicity potential of the substance subject to the present decision and, thus, it is justified by the Registrant to generate additional data for this endpoint, in accordance with the provisions of Annex IX, section 8.7.2., column 2. The test conditions shall be modified by pH adjustment.

Therefore, pursuant to Article 40(3)(b) of the REACH Regulation, the Registrant is required to carry out the study: Pre-natal developmental toxicity study in rabbits, oral route (test method: EU B.31/OECD 414) using sodium salt of the registered substance.

ECHA notes that the Registrant has furthermore justified the testing proposal for pre-natal developmental toxicity study with effects on spermatogenesis observed in a 90 day subchronic toxicity study with dogs using the substance sodium trichloroacetate.

ECHA understands from the arguments used by the Registrant that the Registrant is proposing a testing strategy where a pre-natal developmental toxicity study is conducted first and, depending on the outcome of this study, the necessity of the two-generation reproductive toxicity study is considered. However, a pre-natal developmental toxicity study can be used only to classify the substance regarding to developmental toxicity and the study is not expected to provide information on effects on fertility. Therefore, to cover the Registrant's concern regarding fertility ECHA originally requested in the draft decision to the Registrant also a two generation reproductive toxicity study (OECD 414) or an extended one generation reproductive toxicity study (OECD 443) in rats by the oral route. In one proposal for amendment from a Member State Competent Authority it was proposed to withdraw the request for this study. The rational was that effects on fertility ("damage to spermatogenesis") were reported in a 90 day toxicity study with dogs but not in long-term repeated dose toxicity studies with rats. Due to this species difference, it was concluded that a generation reproductive toxicity study in rats might not be suitable to conclude on the concern for fertility. Consequently the Member State Committee meeting decided to remove this request from the decision.

However, the concern on fertility still remains and the Registrant is required by the REACH Regulation to take that concern into account for instance through the application of appropriate risk management measures and/or the development and implementation of a testing strategy to further understand and interpret the findings in the dog study. The Registrant is reminded that if testing according to Annex IX or X of the REACH Regulation needs to be performed, a new testing proposal will need to be submitted to the Agency.

IV. Adequate identification of the composition of the tested material

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.

Furthermore, there must be adequate information on substance identity for the sample tested and the grades 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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Geert Dancet
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