ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-0000003575-70-03/F Helsinki, 31 July 2013

DECISION ON A COMPLIANCE CHECK OF A REGISTRATION PURSUANT TO ARTICLE 41(3) OF REGULATION (EC) NO 1907/2006

For 2,2',2''-nitrilotriethanol, CAS No 102-71-6 (EC No 203-049-8), 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 41(1) of the REACH Regulation ECHA has performed a compliance check of the registration dossier for 2,2',2''-nitrilotriethanol, CAS No 102-71-6 (EC No 203-049-8, submitted by [redacted] (Registrant), latest submission number [redacted], for the tonnage band of 1000 tonnes or more per year.

The scope of this compliance check is limited to the standard information requirements of Annex VII, Sections 8.4.1 and 9.1.2 and Annex IX, Section 9.1.5 of the REACH Regulation.

This decision does not take into account any updates after 20 June 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 compliance check decision does not prevent ECHA from initiating further compliance checks on the present dossier at a later stage.

The compliance check was initiated on 21 February 2013.

On 26 April 2013 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision. That draft decision was based on submission number [redacted].

On 24 May 2013 ECHA received comments from the Registrant not agreeing with the draft decision.

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

On 20 June 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 did not propose amendments to the draft decision and ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

II. Information required

Pursuant to Articles 41(1)(a), 41(3), 10(a)(vii), 12(1)(e), 3(28) and 13(3)-(4) and 111 as well as Annex XI, 1.1.2 of the REACH Regulation the Registrant shall submit for the registered substance:

1. Mutagenicity, *in vitro* gene mutation study in bacteria with an additional, fifth strain of bacteria (Annex VII, 8.4.1.) following an up-to-date EU Method B.13/14 (OECD Test Guideline 471);
2. Robust study summary in the IUCLID format for long-term toxicity testing on aquatic invertebrates (Annex IX, 9.1.5), as specified in Section III.2 below.
3. Robust study summary in the IUCLID format for growth inhibition study on aquatic plants (Annex VII, 9.1.2.; test method: EU C.3./OECD 201), as specified in Section III.3 below.

Pursuant to Article 41(4) of the REACH Regulation the Registrant shall submit the information in the form of an updated IUCLID dossier to ECHA by **31 January 2014**.

III. Statement of reasons

Pursuant to Article 41(3) of the REACH Regulation, ECHA may require the Registrant to submit any information needed to bring the registration into compliance with the relevant information requirements.

Based on the examination of the technical dossier and the Registrant's comments, ECHA concludes that the information therein, submitted by the Registrant for registration of the above mentioned substance for the purpose of registration within the applicable tonnage band of 1000 tonnes or more per year in accordance with Article 6 and 11(2) of the REACH Regulation, does not comply with the requirements of Articles 10, 12 and 13 and with Annexes VII to XI thereof. Consequently, the Registrant is requested to submit the information mentioned above that is needed to bring the registration into compliance with the relevant information requirements.

1. Mutagenicity, *in vitro* gene mutation study in bacteria with an additional, fifth strain of bacteria

Pursuant to Articles 10(a)(vi) and (vii), 12(1)(e) of the REACH Regulation, a registration for a substance produced in quantities of 1000 tonnes or more per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

An in vitro gene mutation study in bacteria is a standard information requirement of section 8.4.1 of Annex VII.

According to Article 13(3) of the REACH Regulation, tests required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods recognised by the Commission or ECHA. Other tests may be used if the conditions of Annex XI are met.

Other tests may be used if the conditions of Annex XI are met. More specifically, Section 1.1.2 of Annex XI provides that existing data on human health properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3) may be used if the following conditions are met:

(1) Adequacy for the purpose of classification and labelling and/or risk assessment;
(2) Adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3);
(3) Exposure duration comparable to or longer than the corresponding test methods referred to in Article 13(3) if exposure duration is a relevant parameter; and
(4) adequate and reliable documentation of the study is provided.

In the present case, ECHA notes that for the standard information requirement of section 8.4.1 of Annex VII, the Registrant has provided data from an *in vitro* gene mutation study in bacteria performed in 1986 on *Salmonella typhimurium* according to OECD test guideline 471 in force at that time and in accordance with the OECD good laboratory practice (GLP) principles.

The test submitted was carried out according to GLP and to OECD guideline 471. However, since the test was conducted, significant changes have been made to OECD guideline 471 and this means that the study does not meet the current guidelines, nor can it be considered as providing equivalent data according to the criteria in Annex XI.

The version of the EU test method B.13/14 or OECD test guideline 471 in force since 1997 introduces the need for performing the test in at least 5 strains of bacteria whereas OECD guideline 471 in force in 1986 only required testing in a minimum of 4 bacterial strains. The required 5th bacterial strain, i.e. *Escherichia coli WP2* strains or *S. typhimurium TA102*, has the potential to detect certain types of mutagens, such as cross-linking agents or oxidising mutagens, which the 4 bacterial strains recommended in the former version of OECD guideline 471 may not detect.

In his comments of 24 May 2013 to the draft decision communicated to the Registrant, the Registrant stated that he has become aware of other available studies on registered substance performed with the requested *E. coli WP2*. The Registrant proposed to include these data in the IUCLID dossier and amend the robust study summary accordingly. ECHA points out that no such dossier update has been received until 20 June 2013, the date of referral of the draft decision to the Member State Competent Authorities, and the information gap remains.

Consequently, in the absence of the above update of the dossier, the Registrant is required to complete the data set on mutagenicity by submitting an *in vitro* gene mutation study in bacteria (Annex VII, 8.4.1) using one missing bacterial strain which may detect mutagens, such as cross-linking agents or oxidising mutagens, i.e. one *E. coli WP2* strain or *S. typhimurium TA102*, following recommendations of EU test method B.13/14 laid down in Commission Regulation (EC) No 440/2008 or OECD test guideline 471 on the registered substance.

Therefore, pursuant to Article 41(1)(a) and (3) of the REACH Regulation, the Registrant is requested to submit the following information derived with the substance subject to the present decision: Bacterial reverse mutation test (test method: EU B.13/14. / OECD 471) using one of the following strains: *E. coli WP2 uvrA*, or *E. coli WP2 uvrA* (pKM101), or *S. typhimurium TA102*.

2. Robust study summary in the IUCLID format for long-term toxicity testing on aquatic invertebrates

According to column 1 of Section 9.1.5. of Annex IX of the REACH Regulation, long-term toxicity testing on invertebrates is required to fulfil the standard information requirements.

Article 13(4) of the REACH Regulation provides 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 required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods recognised by the Commission or ECHA. Other tests may be used if the conditions of Annex XI are met. More specifically, Section 1.1.2 of Annex XI provides that existing data on environmental properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3) may be used if the following conditions are met:

(1) Adequacy for the purpose of classification and labelling and/or risk assessment;
(2) Adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3);
(3) Exposure duration comparable to or longer than the corresponding test methods referred to in Article 13(3) if exposure duration is a relevant parameter; and
(4) adequate and reliable documentation of the study is provided.

According to Articles 10(a)(vii) and 111 and Section and 3.1.5 of Annex I to the REACH Regulation, a technical dossier that is in the IUCLID format shall include robust study summaries of all key data used in environmental hazard assessment. Under Article 3(28), the robust study summary shall include a "detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report."

In the present case, ECHA notes that a robust study summary for a study flagged as a key study (IUCLID section 6.1.4: 'Kuehn et al. 1989. Long-term toxicity to aquatic invertebrates') is available for the registered substance. The test has not been conducted in accordance with the recommended standard method OECD 211.

In his comments of 24 May 2013 to the draft decision communicated to the Registrant, the Registrant provided additional information on the reliability of the study and documentation. This additional information appears sufficient for ECHA to consider that the study by Kuhn et at 1989 is a valid study within the meaning of Articles 13(3) - (4) and Annex XI, Section 1.1.2 of the REACH Regulation and the NOEC of 16 mg/L can be used for the PNEC derivation and for confirming that no environmental classification and labelling is needed.

ECHA, however, points out that until 20 June 2013, it has not received a dossier update addressing the above comments and therefore the information gap regarding the robust study summary remains. More specifically, contrary to Article 3(28) of the REACH Regulation, the robust study summary still contains no information – apart from the 21-day NOEC – in the 'Results and discussions', 'Overall remarks', 'attachments', and 'Applicant's summary and conclusion' section. For instance, no information is provided on the number of offspring, dose-response relationship, description of statistical analysis.

Therefore, pursuant to Articles 41(1)(a), 41(3), 3(28),10(a)(vii) and 111 of the REACH Regulation, the Registrant is requested to provide a robust study summary containing the above missing information in the IUCLID format of the study marked as a key study listed above.

Further guidance on the reporting requirements can be found in the 'Practical guide 3: How to report robust study summaries' published on ECHA website at: http://echa.europa.eu/documents/10162/17235/pg_report_robust_study_summaries_en.pdf.

3. Robust study summary in the IUCLID format for growth inhibition study on aquatic plants

According to column 1 of Section 9.1.2. of Annex VII of the REACH Regulation, toxicity testing on aquatic plants is required to fulfil the standard information requirements.

According to Articles 10(a)(vii) and 111 and Section and 3.1.5 of Annex I to the REACH Regulation, a technical dossier that is in the IUCLID format shall include robust study summaries of all key data used in environmental hazard assessment. Under Article 3(28), the robust study summary shall include a "detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report."

ECHA observes that one key study is available for the registered substance for the present endpoint (IUCLID section 6.1.5: 'Key. Amann 1989. Toxicity to aquatic algae and cyanobacteria')).

In his comments of 24 May 2013 to the draft decision communicated to the Registrant, the Registrant provided additional information on the use of neutralised values and that the substance and study results are not of concern. The Registrant also stated that the study has been peer-reviewed by the German Commission for the Evaluation of Substances hazardous to waters (KBwS), which consists of representatives of the federal and state governments, industry and further experts, although the results of this peer review are not provided in the registration dossier.

ECHA, however, points out that until 20 June 2013 it has not received a dossier update addressing the above comments and therefore the information gap regarding the robust study summary remains. More specifically, contrary to Article 3(28) of the REACH Regulation, the robust study summary of the key study still does not contain sufficient information – apart from the effect values – in the 'Results and discussions', 'Overall remarks', 'attachments', and 'Applicant's summary and conclusion' section. For instance, no information is provided on observations (biomass, growth rate), growth curves (including evidence of exponential growth in the controls), other effects (microscopic appearance, size, shape of the cells). Such data should be included in the robust study summary. Further, the Registrant is requested to include his explanation on the use of neutralised values and that the substance and study results are not of concern in the robust study summary.

Therefore, pursuant to Articles 41(1)(a), 41(3), 3(28),10(a)(vii) and 111 of the REACH Regulation, the Registrant is requested to provide a robust study summary containing the above missing information in the IUCLID format of the study marked as a key study listed above.

Further guidance on the reporting requirements can be found in the 'Practical guide 3: How to report robust study summaries' published on ECHA website at: http://echa.europa.eu/documents/10162/17235/pg_report_robust_study_summaries_en.pdf.

Deadline for submitting the information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 12 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 long-term toxicity study on aquatic invertebrates (Annex IX, 9.1.5 of the REACH Regulation). As this information requirement has been removed on the basis of the Registrant's comments of 24 May 2013, ECHA considers that a reasonable time period for providing the required information in the form of an updated registration is six months from the date of the adoption of the decision. The decision was therefore modified accordingly.

IV. Adequate identification of the composition of the tested material

In relation to the information required by the present decision, 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 who manufacture or import the same substance to agree on the appropriate composition of the test material 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 an appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on 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
Executive Director