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European Chemicals Agency

For final decision: CCH-D-0000001796-64-04/F Helsinki, 23 November 2011

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

For *Ethanol, 2-methoxy-, manufacture of, by-products from, esters with boric acid*, CAS 161907-80-8 (EC No 310-290-3), 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 41(1) of the REACH Regulation the ECHA has performed a compliance check of the registration dossier for ***ethanol, 2-methoxy-, manufacture of, by-products from, esters with boric acid***, CAS 161907-80-8 (EC No 310-290-3) submitted by [redacted] (the Registrant), latest submission number [redacted], for > 1000 tonnes per year.

The compliance check was initiated on 18 March 2011.

On 29 April 2011 ECHA notified the Registrant of its draft decision and invited him pursuant to Article 50(1) of the REACH Regulation to provide comments within 30 days of the receipt of the draft decision.

On 27 May 2011 the Registrant provided to ECHA comments on the draft decision. On 1 July 2011 the Registrant submitted an updated dossier.

ECHA reviewed the further information received and amended the draft decision accordingly.

On 29 July 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.

Subsequently, one Competent Authority of the Member States submitted a proposal for amendment to the draft decision.

On 31 August 2011 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 within 30 days of the receipt of the notification.

ECHA reviewed the proposal for amendment received and did not modify the draft decision.

On 12 September 2011, the draft decision was referred to the Member State Committee.

The Registrant did not provide any comments on the proposal for amendment.

A unanimous agreement of the Member State Committee on the draft decision was reached on 14 October 2011 in a written procedure launched on 3 October 2011.

This compliance check decision does not prevent ECHA to initiate further compliance checks on the present dossier at a later stage.

II. Information required

1) Pursuant to Articles 41(1)(a) and 10(a)(ii) as well as Annex VI, section 2 of the REACH Regulation the Registrant shall submit for the registered substance:

   a. Name or other identifier of each substance (Annex VI, 2.1), more specifically details on the identity of the starting materials and on the manufacturing process: Information which is suitable and necessary to allow ECHA to establish and verify the name of the registered substance, as specified under section III.1)(a) below;
   b. The composition (Annex VI, 2.3.): Information which is suitable and necessary to allow ECHA to establish and verify the composition and the name of the registered substance, as specified under section III.1)(b). below; and
   c. The description of analytical method or the appropriate bibliographic references used for the quantification of the registered substance (Annex VI, 2.3.7.). The information shall be sufficient for each method to be reproduced and shall therefore include details of the experimental protocol followed, the calculation used and the result obtained.

2) Pursuant to Articles 41(1)(a) and (b), 10(a)(vi) and (vii), 12(1)(e), 13 and Annexes VII-IX and XI of the REACH Regulation, the Registrant shall submit:

   a. A justification detailing and documenting, as further specified under section III.2) below, why the testing done on another substance than the registered substance would fulfil the information requirements of Annexes VII-IX, for the following endpoints: acute oral toxicity (Annex VII, 8.5.1), acute dermal toxicity (Annex VIII, 8.5.3), skin irritation (Annex VIII, 8.1.1), eye irritation (Annex VIII, 8.2.1), skin sensitisation (Annex VII, 8.3), short-term repeated dose toxicity (28 days) (Annex VIII, 8.6.1), *in vitro* cytogenicity study in mammalian cells (Annex VIII, 8.4.2), screening developmental toxicity, short-term toxicity on *Daphnia* (Annex VII, 9.1.1), algae growth inhibition (Annex VII, 9.1.2) and short-term toxicity on fish (Annex VIII, 9.1.3).

3) Pursuant to Articles 41(1)(a) and (b), 10(a)(vi) and (ix), 12(1)(e), 13 and Annexes VIII- IX and XI of the REACH Regulation, the Registrant shall submit:

a. A justification detailing and documenting, as further specified under section III.3) below, why the testing proposed for sub-chronic toxicity (90 days), pre-natal developmental and two-generation reproductive toxicity tests, intended to be carried out on another substance than the registered substance, would fulfil the information requirements of Annex IX, 8.6.2 and 8.7.2, and Annex X, 8.7.3. for the registered substance,
b. A justification detailing and documenting, as further specified under section III.3) below, why the *in vitro* gene mutation study in mammalian cells carried out on another substance than the registered substance, would fulfil the information requirement of Annex VIII, 8.4.3., for the registered substance,

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 23 February 2012.

III. Statement of reasons

Based on the examination of the technical dossier, ECHA concludes that the information therein, submitted by the Registrant for registration of the above mentioned substance in accordance with Article 6 of the REACH Regulation, does not comply with the requirements of Articles 10, 12 and 13 and with Annexes VI, VII-X, and 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) Missing information related to substance identity

Pursuant to Article 10(a)(ii) and Annex VI, section 2 of the REACH Regulation, the technical dossier of the registration shall include information on the identity of the substance. Annex VI, section 2 lists information requirements that shall be sufficient to identify the registered substance.

a. Name or other identifier of each substance (Annex VI, 2.1):

The registered substance has been identified as an UVCB substance and named according to the manufacturing process. For this type of substance the chemical name and the composition are not sufficient for substance identification. Additional information such as identity of the starting materials and information on the manufacturing process are also essential identifiers for the identification of the substance. The identity of the one reactant (MTTO) reported in section 3.1 of the IUCLID dossier is unclear. The registrant indicates this starting material as consisting mainly of TEGME (tris{2-[2-(2-methoxyethoxy)ethoxy]ethyl} borate) and TetraEGME (tris(3,6,9,12-tetraoxatridec-1-yl) borate), however according to the composition reported in section 1.2 another constituent (tris[2-[2-[2-[2-(2-Methoxyethoxy)ethoxy]ethoxy]ethyl]]orthoborate, concentration up to [redacted]) may also be regarded as a predominant in the composition.
Therefore ECHA concludes that the provided information is not sufficient to identify the substance.

In response to ECHA's draft decision, the Registrant updated the dossier in which the ratio of the reactants (= starting material) and partial composition of the main reactant as requested in the draft decision was provided.

However, the composition of the one reactant (TTEGME/MTTO) reported in section 3.1 of the updated IUCLID dossier is still not complete. The Registrant indicates this starting material as consisting mainly of 2-(2-(2-methoxyethoxy)ethoxy)ethanol ([redacted]), 3,6,9,12-tetraoxotridecanol ([redacted]) and in lower concentrations 3,6,9,12,15-pentaoxahexadecanol [redacted] and 3,6,9,12,15, 18-nonadecanol [redacted]). The sum of the minimum concentration of the major constituent and maximum concentration of three others ([redacted]) would however indicate that [redacted] of the starting material stays unknown and other constituents could be potentially present.

Accordingly, the Registrant shall revise the composition of the starting material, report any other constituent present and/or provide more narrow concentration ranges. This information should be included in the description field in section 1.1 of the IUCLID dossier. The Registrant should ensure that the information on the relevant steps taken during the manufacturing process reported in section 3.1 is consistent with the description field in section 1.1 of the IUCLID dossier.

b. Composition of the registered substance (Annex VI, 2.3.):

The substance composition corresponds to the chemical representation of what the substance consists of and is therefore an essential part of substance identification and the corner stone of all the REACH obligations.

ECHA notes that the registration does not contain sufficient information for establishing the composition of the registered substance and therefore its identity, as required under Annex VI, Section 2.3. of the REACH Regulation. More specifically the composition of the substance given in the section 1.2 of IUCLID dossier is not consistent with the analytical report provided in section 1.4. The composition in section 1.2 consists of only 3 boric acid esters and 2 impurities, whereas in the analytical report 8 different esters (including 3 already reported in section 1.2) were identified using mass spectroscopy. Moreover, concentration ranges provided in section 1.2 ([redacted]) are very broad, which has not been justified by the specific manufacturing process conditions or starting materials properties. Furthermore the concentration ranges of three main constituents are also not consistent with the ranges specified in the analytical report ([redacted]).
Therefore, the substance identity, including the chemical name, could not be verified. In addition, the composition given in section 1.2 of the IUCLID dossier cannot be confirmed as the results of the quantitative analysis have not been provided (as specified in point 1)(c) below).

Following section 4.3 of the Guidance for identification and naming of substances under REACH http://guidance.echa.europa.eu/docs/guidance_document/substance_id_en.pdf, the Registrant should note that for UVCB substances (substances of Unknown, or Variable Composition, or of Biological origin) such as the registered substance, the following applies:

- All constituents present in the substance with a concentration of ≥ 10 % shall be identified and reported individually, and

- All constituents relevant for the classification and/or PBT assessment of the registered substance shall be identified and reported individually; and
- Any other known constituent should also be specified and their typical concentration and concentration range be indicated; and
- Unknown constituents should, whenever possible, be identified by a generic description of their chemical nature.

In line with the above, the Registrant is requested to provide any information which is suitable and necessary to allow ECHA to establish and verify the composition of the registered substance.

In response to ECHA's draft decision, the Registrant updated the dossier in which information on the residual alcohols in the composition of the registered substance was provided. In addition, in his comments the Registrant clarified that butanol is not a part of the substance.

However, the composition of the registered substance is still not consistent with the analytical report. Only 3 boric acid esters and 2 impurities are listed in the composition, whereas in the analytical report 8 different esters (3 of them already included in the composition reported in section 1.2) were identified using mass spectroscopy. Moreover, concentration ranges ([redacted]) are still very broad, which has not been justified by the specific manufacturing process conditions or starting materials properties. Furthermore the concentration ranges of three main constituents are also not consistent with the reasonably narrow ranges specified in the analytical report ([redacted]).

Therefore, ECHA concludes that the Registrant is still requested to revise the composition in line with the analytical data and to provide more narrow concentration ranges.

Regarding how to report the composition of the registered substance in IUCLID, the following applies: The Registrant should report the composition of the registered substance in IUCLID section 1.2. For each constituent required to be reported individually, the IUPAC name, CAS name and CAS number (if available), molecular and structural formula, as well as the minimum, maximum and typical concentration, shall be reported in the appropriate fields in IUCLID.

For the other constituents to be reported under a generic description, a generic chemical name describing the group of constituents, generic molecular and structural information (if applicable), the carbon number range, as well as the minimum, maximum and typical concentration, shall be reported in the appropriate fields in IUCLID.

If it is technically impossible to determine the exact quantitative composition including all possible boric acid esters ($(MeO-(CH_2CH_2O)_n)_3B$ where n=3,4,5) the Registrant can alternatively create one generic reference substance covering every possible combination of boric acid esters and provide in the remarks field the relative concentration of tri, tetra and penta $-CH_2CH_2O-$ units in the substance.

Further technical details on how to report the composition of UVCB substances in IUCLID are available in paragraphs 2.1 and 2.2.2 of the Data Submission Manual 18 on the ECHA website at:
http://echa.europa.eu/doc/reachit/dsm18/substance_id_report_iuclid_en.pdf.

c. The description of the analytical methods or the appropriate bibliographical references for the identification of the substance (Annex VI, 2.3.7.):

ECHA notes that the registration does not contain sufficient details of the analytical methods to identify the registered substance, including its composition, as required by Annex VI, 2.3.7. of the REACH Regulation. The registrant provided results of the spectroscopic analysis (IR, UV, NMR and MS) for identification of the registered substance. However, no quantitative method is indicated to prove the composition and therefore identity of the substance. Instead, the Registrant includes justifications for not providing gas (GC) or high performance liquid chromatograms (HPLC).
Therefore it is not clear how the concentration ranges for the different constituents listed in section 1.2 of the IUCLID dossier have been derived by the Registrant.

Accordingly, in line with Annex VI, 2.3.7., the Registrant is requested to submit the description of the missing analytical methods, or the appropriate bibliographical references, to identify the registered substance, including its composition. The information shall be sufficient for each method to be reproduced and shall therefore include details of the experimental protocol followed, the calculation used and the result obtained. If the substance was quantified by the indirect methods (derivatization) or the composition was derived based on the starting material, the detailed description of such analysis, results and calculations used shall be provided.

As for the reporting of the above data in the registration dossier, the information should be attached in IUCLID section 1.4.

2) Missing information related to the endpoints concerned

a. Missing information concerning the use of read-across

In response to ECHA's draft decision, the Registrant updated the dossier with a read-across justification regarding the studies conducted with the read-across substance, [redacted]: acute oral toxicity (Annex VII, 8.5.1), acute dermal toxicity (Annex VIII, 8.5.3), skin irritation (Annex VIII, 8.1.1), eye irritation (Annex VIII, 8.2.1), skin sensitisation (Annex VII, 8.3), short-term repeated dose toxicity (28 days) (Annex VIII, 8.6.1), *in vitro* cytogenicity study in mammalian cells (Annex VIII, 8.4.2), screening developmental toxicity, short-term toxicity on *Daphnia* (Annex VII, 9.1.1), algae growth inhibition (Annex VII, 9.1.2) and short-term toxicity on fish (Annex VIII, 9.1.3).

ECHA evaluated the justification for read-across from [redacted] submitted by the Registrant and the preliminary conclusion is that the criteria according to Annex XI, section 1.5 are met.

However, the decision on the acceptability of the read-across justification regarding the above endpoints depends on the substance identity information, i.e. the components of the registered substance as specified in point 1) need to correspond to the ones that are presented in the read-across justification. Without the necessary information on the

identity of the registered substance the similarity of substances, as required under Annex XI, section 1.5, cannot be fully assessed. Therefore, the decision on the acceptability of the read-across approach to fulfil the information requirements of specified above endpoints of Annexes VII and VIII can only be made after the Registrant has updated the dossier with the information requested in point 1).

3) Missing information concerning the use of read-across approach

ECHA notes that

a. the Registrant intends to cover the information requirements of the sub-chronic, pre-natal developmental and two-generation reproductive toxicity studies (standard requirements of Annex IX, 8.6.2 and 8.7.2, and Annex X, 8.7.3, respectively) by performing the tests according to the OECD guidelines 408, 414 and 416, respectively, and proposes to perform these tests with a read-across substance, [redacted], and

b. *in vitro* gene mutation study in mammalian cells present in the dossier has been conducted with the same read-across substance, [redacted]

In response to ECHA's draft decision, the Registrant updated the dossier with the read-across justification regarding the above endpoints.
ECHA evaluated the justification for read-across from [redacted] submitted by the Registrant and the preliminary conclusion is that the criteria according to Annex XI, section 1.5 are met.

However, the decision on the acceptability of the read-across justification regarding the mutagenicity study and the decision on the substance to be tested following testing proposal examination depends on the substance identity information, i.e. the components of the registered substance as specified in point 1) need to correspond to the ones that are presented in the read-across justification. Without the necessary information on the identity of the registered substance the similarity of substances, as required under Annex XI, section 1.5, cannot be fully assessed. Therefore, the decision on the acceptability of the read-across approach to fulfil the information requirements of specified above endpoints of Annexes VIII-X can only be made after the Registrant has updated the dossier with the information requested in point 1).

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 reads:

> "Ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice provided for in Directive 2004/10/EC or other international standards recognised as being equivalent by the Commission or the Agency and with the provisions of Directive 86/609/EEC, if applicable."

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 the technical progress and use the applicable test methods to generate the information on the endpoints indicated above.

National authorities monitoring good laboratory practice (GLP) maintain lists of test facilities indicating the relevant areas of expertise of each facility.

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 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.

Done at Helsinki,

[redacted]

Jukka Malm
Director of Regulatory Affairs