EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-0000005226-77-02/F Helsinki, 16 September 2014

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

For 1-propanaminium, 3-amino-n-(carboxymethyl)-n,n-dimethyl-, n-c8-18(even numbered) acyl derivs., hydroxides, inner salts, EC No 931-296-8, 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 for 1-propanaminium, 3-amino-n-(carboxymethyl)-n,n-dimethyl-, n-c8-18(even numbered) acyl derivs., hydroxides, inner salts, EC No 931-296-8, submitted by [redacted] (Registrant). The scope of this compliance check is limited to the standard information requirement of Annex VI, Sections 4.1 and 4.2 relating to classification and labelling for aquatic hazard. ECHA stresses that it has not checked the information provided by the Registrant and other joint registrants for compliance with the requirements regarding the identification of the substance (Section 2 of Annex VI) or those of Annexes VII to IX relating to aquatic toxicity.

This decision is based on the registration as submitted with submission number [redacted], for the tonnage band of 1000 tonnes or more per year. This decision does not take into account any updates submitted after 12 June 2014, 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 registration at a later stage.

The compliance check was initiated on 17 June 2013.

On 15 July 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 13 August 2013 ECHA received comments from the Registrant on the draft decision. On 18 December 2013 the Registrant updated his registration dossier with the submission number [redacted]

The ECHA Secretariat considered the Registrant's comments and update.
The information is reflected in the Statement of Reasons (Section III) whereas no amendments to the Information Required (Section II) were made.

On 12 June 2014 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 for amendment of the draft decision within 30 days of the receipt of the notification.

As no proposal for amendment was submitted, 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)(iv) and Annex VI, sections 4.1. and 4.2. of the REACH Regulation in conjunction with Title I and II of Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures (CLP Regulation) the Registrant shall submit the following information for the registered substance subject to the present decision:

- the hazard classification of the registered substance for acute aquatic toxicity Category 1 based on Title I and II of Regulation (EC) No 1272/2008 (CLP Regulation) and resulting hazard statement in line with the criteria set out in Part 4 of Annex I of the CLP Regulation, as amended by Commission Regulation (EU) No 286/2011 of 10 March 2011 (Tables 4.1.0. (a) and 4.1.4), as specified in section III below. In the alternative, the Registrant is required to provide reasons why no such classification is given.

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 **23 December 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 requirement. The scope of the present decision is limited to classification and labelling for aquatic toxicity (Annex VI, Sections 4.1 and 4.2 of the REACH Regulation).

Lack of coherence between the data on aquatic toxicity and the hazard classification included in the dossier:

Pursuant to Article 10(a)(iv) and Annex VI, section 4 of the REACH Regulation, the technical dossier of the registration shall include information on the classification and labelling of the substance. Annex VI, section 4.1 clarifies that the hazard classification of the substance shall result from the application of Title I and II of the CLP Regulation. In addition, for each entry, reasons why no classification is given for a hazard class or differentiation of a hazard class should be provided. According to Article 5(1) of Title I and recitals 20 and 21 of the CLP Regulation, a substance shall be classified on the basis of available information.

Furthermore, the technical dossier must include the resulting hazard label for the substance in line with Title III of the CLP Regulation (Annex VI, section 4.2 of the REACH Regulation).

In the present case, ECHA notes the following:

The technical dossier includes an aquatic acute toxicity study indicating an $L(E)_{50}$ equal to or lower than 1 mg/l which is considered reliable by the Registrant (Klimisch score 1 or 2). However, the Registrant has not classified the substance as Aquatic Acute Hazard Category 1 and used the resulting hazard statement "H400: Very toxic to aquatic life", which would

be in line with the criteria set out in Part 4 of Annex I of the CLP Regulation, as amended by Commission Regulation (EU) No 286/2011 of 10 March 2011 (see Tables 4.1.0. and 4.1.4 of the CLP Regulation).

In his comments submitted on 13 August 2013, the Registrant indicated that the algae study based on which classification would be needed was chosen as the key study by mistake, when their intention was to build a weight-of-evidence (WoE) approach. The Registrant has also submitted a dossier update on 18 December 2013 with submission number [redacted]. In the updated dossier the WoE approach for the endpoint of Growth inhibition study aquatic plants (algae preferred; Annex VII, 9.1.2.) has been applied. ECHA notes that the Registrant has selected four studies for the WoE (EC50s ranging from 0.74 to 9.86 mg/L). ECHA notes that in the WoE the Registrant has used a read-across and grouping approach based on Annex XI, 1.5. of the REACH Regulation. Three of the algae studies submitted are read-across studies with Coco AAPB (IUPAC name: 1-Propanaminium, 3-amino-N-(carboxymethyl)-N,N-dimethyl-, N-(C8-18 (even numbered), C18 unsaturated acyl) derivs., hydroxides, inner salts; EC No 931-333-8, CAS No. 147170-44-3) as the test substance whereas one study is read-across from C12 AAPB (IUPAC name: 1-Propanaminium, N-(carboxymethyl)-N,N-dimethyl-3-[(1-oxododecyl)amino]-, inner salt; EC No 224-292-6, CAS No 4292-10-8).

ECHA has analysed the proposed read-across approach as used in the WoE approach in the endpoint of Growth inhibition study aquatic plants (algae preferred; Annex VII, 9.1.2.) only. ECHA notes that it did not evaluate the read-across used in any other endpoints for compliance with the REACH information requirements. For this read-across assessment only the read-across between two analogues and the target substance has been evaluated, but not the grouping of all five analogues which is presented in the technical dossier for the registered substance. Such evaluation may be carried out in a compliance check under Article 41 of the REACH Regulation at a later stage.

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated by means other than tests. Such other means include the use of information from structurally related substances (grouping of substances and read-across), "*provided that the conditions set out in Annex XI are met*". As far as the WoE approach used for the endpoint of Growth inhibition study aquatic plants is concerned, the Registrant has described an analogue approach of related substances and proposes to use information from two members of this analogue aproach to predict the toxicity to algae for the registered substance using read-across and WoE approach.

ECHA has considered the documentation and the scientific validity of the proposed read-across and grouping approach for the WoE in question. It is a requirement of Annex XI, 1.5., that "*adequate and reliable documentation of the applied method shall be provided.*" ECHA considers that for the endpoint algal toxicity the hypothesis for grouping the substances together is clearly described by the Registrant. Overall the documentation can be regarded as sufficient according to the requirement in Annex XI, 1.5.

Section 1.5. of Annex XI states: 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. ECHA notes that in the current case, the Registrant did not use a group approach but an one-to-one analogue approach. For the analogue approach Annex XI, 1.5. provides:
The similarities may be based on:

(1) a common functional group;
(2) the common precursors and/or the likelihood of common breakdown products via

physical and biological processes, which result in structurally similar chemicals; or
(3) a constant pattern in the changing of the potency of the properties across the category.

Ad (1) and (2): Alkylamidopropyl betaines (AAPBs) are UVCB substances which are defined as reaction products of natural fatty acids or oils with dimethylaminopropylamine and further reaction with sodium monochloroacetate. As their origin is from natural sources, the used fatty acids may have a mixed slightly varying composition with an even numbered chain length from C8 to C18. Unsaturated C18 amounts may be included. The AAPBs differ by their carbon chain length distribution and the degree of unsaturation in the fatty acid moiety. However, Lauramidopropyl betaine (C12 fatty acid derivate) is the major ingredient of all AAPBs. The major constituents of the substances share the same functional groups. The only difference is the carbon chain length and unsaturated bonds for C18. Therefore the same reactivity of the analogues can be reasonably assumed.

Ad (3): For all three analogues rather similar lipophilicity (logKow) can be expected based on the nature and concentration of the main constituents. C8-18 and C18 unsatd. AAPB (Coco AAPB) and the registered substance C8-C18 AAPB both can contain significant amounts of C18 compared to C12 AAPB. Therefore aquatic toxicity might be lower for C12 AAPB. Read-across from C8-C18 AAPB and Coco AAPB to C12 AAPB would be possible as it appears to be conservative. Read-across from C12 AAPB to the other two analogues may potentially underestimate aquatic toxicity. Furthermore, the water solubility of C12 AAPB is different compared to C8-C18 AAPB and Coco AAPB. Unsaturated C18 can be expected to have a slightly lower logKow compared to C18. Overall, similar aquatic toxicity can be expected between Coco AAPB and the registered substance, therefore read-across is plausible between these two analogues.

In conclusion, ECHA considers that the read-across approach used in the WoE for the endpoint of Growth inhibition study aquatic plants (algae preferred; Annex VII, 9.1.2.) is acceptable. However, ECHA would like to highlight that the geometric mean applied by the Registrant is not acceptable as outlined below.

ECHA notes that the Registrant has in fact submitted eight studies for the endpoint of toxicity to algae, four have been used for the WoE, four have been marked as supporting studies. As also stated by the Registrant, the results vary considerably. It is not clear to ECHA why the four studies have been selected for the WoE approach. The Registrant has then calculated a geometric mean of the effect values and used this as the Key value for the chemical safety assessment for the endpoint of toxicity to algae.

According to the CLP guidance chapter 4.1.3.2.4 (Guidance on the Application of the CLP Criteria, Version 4.0, November 2013), and as also pointed out by the Registrant in his comment, the geometric mean of toxicity values may be used as the representative toxicity value for that species when larger data sets (four or more values) are available for the same species. However, ECHA notes that only three of the studies in the WoE have used *Desmodesmus subspicatus* (freshwater green algae) as the test species whereas in the study showing the highest concern *Skeletonema costatum* (marine red tide microalgae) was the test species. ECHA therefore concludes that as different species were used in the WoE-approach applied by the Registrant, the WoE is not valid for classification purposes. Consequently the study showing the highest concern should be chosen as the key study for classification purposes and the substance should be classified accordingly.

Therefore, the Registrant is requested to submit a hazard classification for aquatic toxicity of the registered substance which results from the application of Title I and II of the CLP

Regulation as specified above and is consistent with the data on aquatic toxicity available in the registration dossier. The Registrant shall also provide resulting hazard statement in line with the criteria set out in Part 4 of Annex I of the CLP Regulation, as amended by Commission Regulation (EU) No 286/2011 of 10 March 2011 (Tables 4.1.0. (a) and 4.1.4). In the alternative, the Registrant is required to provide reasons why no such classification is given.

ECHA notes that in reviewing whether the Registrant has complied with Sections 4.1. and 4.2. of Annex VI to the REACH Regulation with regard to classification and labelling for aquatic toxicity, it can only base its assessment on data on aquatic toxicity that is available in the registration dossier. Any other data on aquatic toxicity of the substance that the Registrant does not submit in his registration dossier but that he may need to consider in his classification, cannot be taken into consideration by ECHA. If there is any other data available on aquatic toxicity of the substance, the Registrant is required to include the data in the registration dossier in line with the second introductory paragraph of Annexes VI to X and step 1 of Annex VI to the REACH Regulation.

Notes for consideration by the Registrant:

REACH Guidance (Chapter R10, May 2008, section R.10.2.2) stipulates that geometric mean can only be used from studies derived from one species. Consequently the geometric mean approach applied by the Registrant in the WoE submitted for the endpoint of Growth inhibition study aquatic plants (algae preferred; Annex VII, 9.1.2.) is not acceptable. ECHA hence recommends the Registrant to reconsider the approach of using the geometric mean as the Key value for the chemical safety assessment for the endpoint of toxicity to algae.

IV. 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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