EUROPEAN CHEMICALS AGENCY

~~Confidential~~

Helsinki, 6 August 2020

Addressee: [redacted]

Decision number: CCH-D-2114509943-45-01/F
Substance name: Alkyl Dimethyl Betaine
EC number: 931-700-2
CAS number: NS
Registration number: [redacted]
Submission number subject to follow-up evaluation: [redacted]
Submission date subject to follow-up evaluation: 23 July 2019
Registered tonnage band: 1000+T

DECISION TAKEN UNDER ARTICLE 42(1) OF THE REACH REGULATION

By decision CCH-D-2114376667-32-01/F of 7 December 2017 ("the original decision") ECHA requested you to submit information by 14 June 2019 in an update of your registration dossier.

Based on Article 42(1) of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA examined the information you submitted with the registration update specified in the header above, and concludes that

Your registration still does not comply with the following information requirement(s):

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

You are therefore still required to provide this information requested in the original decision.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. Advice and further observations are provided in Appendix 3.

The respective Member State competent authority (MSCA) and National enforcement authority (NEA) will be informed of this decision. They may consider enforcement actions to secure the implementation of the original decision and exercise the powers reserved to them under Article 126 of Regulation No 1907/2006 (penalties for non-compliance) for the period during which the registration dossier is not compliant[1].

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, shall be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under http://echa.europa.eu/regulations/appeals.

Approved[2] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[1] See paragraphs 61 and 114 of the judgment of 8 May of the General Court of the European Court of Justice in Case T-283/15 Esso Raffinage v. ECHA
[2] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

In the compliance check decision you were requested to submit information derived with the Substance for Sub-chronic toxicity study (90-day), via oral route.

In the updated registration subject to follow-up evaluation, you have applied a read-across approach based on analogue approach and provided experimental studies according to OECD Guideline 408 (Repeated Dose 90-Day Oral Toxicity in Rodents) CAPB (EC 263-058-8) and read-across documentation.

Assessment of the read-across approach

Legal framework

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used.

Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category.

Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[3] and related documents[4, 5].

Information provided

In the compliance check decision you were requested to submit information derived with the registered substance "Betaines, C12-14 (even numbered)-alkyldimethyl" (the Substance). In the updated registration subject to follow-up evaluation, you have applied a read-across approach based on an analogue approach (structurally similar substances will have similar toxicological properties (scenario 2 of RAAF)). You have provided experimental studies with the source substances (Coco betaine, EC 270-329-4; Cetyl betaine, EC 211-748-4; Lauryl betaine, EC 211-669-5; Alkyl (C12-C16) dimethyl ammonio acetate, (mixture of EC 220-006-9 and EC 211-669-5); and CAPB, EC 263-058-8) and you have provided read-across justification documentation.

Evaluation of the adaptation

ECHA has assessed your adaptation in light of the requirements of Annex XI, Section 1.5 of the REACH Regulation and considers that the read-across cannot be accepted for the reasons presented below.

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[3] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals. 2008 (May) ECHA, Helsinki. 134. pp. Available online: https://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf/77f49f81-b76d-40ab-8513-4f3a533b6ac9

[4] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)

[5] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: https://doi.org/10.2823/794394

Information contradicting your read-across hypothesis

Annex XI, Section 1.5. provides that "substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances. The ECHA Guidance[6] indicates that "*it is important to provide supporting information to strengthen the rationale for the read-across*". The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s). The observation of differences in the toxicological properties between the source substance(s) and the Substance is a warning sign. In such circumstances a valid justification needs to be provided why the observed differences do not affect the read-across hypothesis.

You consider that CAPB represents a "*reasonable worst-case substance in terms of oral absorption and subsequent systemic toxicity*" based on the presence of an amidopropyl group in its structure affecting its physico-chemical properties.

In your technical dossier you have provided results from two 90-day repeated dose toxicity studies conducted with CAPB ([redacted] 1991b and [redacted] 1994) and you use these studies as source studies in your read-across approach.

You have also provided information from OECD TG 422 studies conducted respectively with Lauryl betaine ([redacted] 2005) and with Alkyl (C12-C16) dimethyl ammonio acetate ([redacted] 2009), from a 91-day repeated dose toxicity study conducted with cetyl betaine ([redacted] 1990) and from a 90-day repeated dose toxicity study conducted with coco betaine ([redacted] 1993) as supporting information for your read-across approach.

CAPB differs from the other substances included in this read-across approach and from the constituents of the Substance by the presence in its structure of an amidopropyl group. You consider that this structural feature increases the absorption potential of this substance and assume subsequent higher systemic toxicity. No or limited information on the absorption of the constituents of the Substance is available to compare the potential systemic bioavailability of the substances and support your claim.

Furthermore, higher relative systemic absorption does not necessarily correlate with higher toxicity. Based on the information provided in your dossier, no other evidence of toxicity than local effects in the digestive tract have been observed after oral administration of CAPB ([redacted] 1991b and [redacted] 1994).

However, in the OECD TG 422 study conducted with lauryl betaine ([redacted], 2005), necrosis of the renal tubular epithelium and hyperplasia of the bladder mucosal epithelium were reported in mid- and high dose animals. In addition, local effects in the digestive tract and thymus atrophy, atrophy of the white pulp in spleen and local necrosis of the adrenal gland were reported.

Another OECD TG 422 study on Alkyl (C12-C16) dimethyl ammonio acetate ([redacted] 2009), containing also lauryl betaine, showed test-item related changes in kidneys, urinary bladder, stomach and bone marrow in the mid- and high dose animals and adrenal glands of the high dose female animals.

[6] Guidance on information requirements and chemical safety assessment (version 6.0, July 2017), Chapter R.6, Section R.6.2.2.1.f

ECHA observes that lauryl betaine is the [redacted] constituent of the Substance, representing up to [redacted] of its composition. However, no information is provided or available on the composition of the test material, and in particular of the concentration of lauryl betaine, used in the sub-chronic studies conducted with CAPB. Based on the differences in the toxicological profiles observed between the studies conducted with CAPB and lauryl betaine ECHA considers that CAPB, as tested in the studies presented in your technical dossier, does not constitute a worst-case substance for the Substance.

The available set of data on the [redacted] constituent of the Substance lauryl betaine and the source substance CAPB indicates differences in the toxicological properties of these substances. This contradicts your read-across hypothesis whereby CAPB constitutes a worst-case substance for the Substance. Therefore, you have not demonstrated and justified that the properties of the source substance CAPB and of the Substance are likely to be similar despite the observation of these differences.

Conclusion

For the reasons presented above and on the basis of the information provided in your registration dossier, ECHA considers that there is insufficient support for your proposal that the Substance and the source substance have similar toxicological properties as a result of structural similarity. For these reasons, ECHA considers that your hypothesis is not a reliable basis whereby the properties of the Substance may be predicted from data from the source substance.

In your comments to the draft decision you expressed your belief that the read-across approach addressed in the decision is *"is still valid and scientifically and morally the best option to fulfill the data requirements"*. You acknowledged that other strategies may also be possible, including e.g. using bridging studies or conducting the required study on the Substance, and indicated that you would consider all these options when updating your dossier.

In response, ECHA observes that you have not provided any further information to support your read-across adaptation or any other adaptation possibility.

ECHA therefore considers that the read-across cannot be accepted for the reasons outlined above.

As detailed above, the request in the original decision was not met, and you are still required to provide information on Sub-chronic toxicity study (90-day), via oral route (Annex IX, Section 8.6.2); test method: EU B.26/OECD TG 408 with the Substance.

Appendix 2: Procedural history

In accordance with Article 42(1) of the REACH Regulation, the Agency examined the information submitted by you in consequence of decision CCH-D-2114376667-32-01/F. The Agency considered that this information did not meet one or more of the requests contained in that decision. Therefore, a new decision-making process was initiated under Article 41 of the REACH Regulation.

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft of this decision was notified to the Member States Competent Authorities according to Article 51(1) of the REACH Regulation.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision and invited you to provide comments.

ECHA took into account your comments and did not amend the request(s).

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

2. The Article 42(2) notification for the original decision is on hold until all information requested in the original decision has been received.