ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 23 July 2019

Addressee: [redacted]

Decision number: CCH-D-2114476331-52-01/F
Substance name: Cetrimonium chloride
EC number: 203-928-6
CAS number: 112-02-7
Registration number: [redacted]
Submission number: [redacted]
Submission date: 27/08/2015
Registered tonnage band: Over 1000

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) in a second species (rat), oral route with the registered substance;**

2. **Robust study summary (RSS) for [redacted] (2006), Ready biodegradability (Annex VII, Section 9.2.1.1. in conjunction with Annex I, Section 3.1.5);**

   OR

   Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: CO2 evolution test, OECD TG 301B) or

   Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: MITI test (I), OECD TG 301C) or

   Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Closed bottle test, OECD TG 301D) or

   Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Manometric respirometry test, OECD TG 301F) or

   Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Ready biodegradability – CO2 in sealed vessels (headspace test), OECD TG 310) with the registered substance.

You have to submit the requested information in an updated registration dossier by ***30 July 2020***. You shall also update the chemical safety report, where relevant.

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

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, has to 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.

Authorised[1] by **Claudio Carlon**, Head of Unit, Hazard Assessment

[1] 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. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Pre-natal developmental toxicity studies (test method OECD TG 414) on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

Subsequent to a proposal for amendment (PfA) submitted by one of the Member States Competent Authorities (MSCAs), ECHA notes that the technical dossier contains information on a pre-natal developmental toxicity study ([redacted] 1985) in rabbits by the dermal route using the registered substance.

However, there is no information provided for a pre-natal developmental toxicity study in a second species.

a. Read-across adaptation

We understand that you have sought to adapt the information requirement for a pre-natal developmental toxicity study in a second species according to Annex XI, Section 1.5. of the REACH Regulation.
According to Annex XI, Section 1.5. (indent 4) of the REACH Regulation, adequate and reliable documentation of the applied method shall be provided.

In your dossier you provided the following justification for data waiving: "*A developmental toxicity test in the rabbit is available for C16 TMAC. The study showed no effects on developmental parameters at any of the tested doses. Repeated dose toxicity testing (28 day) was conducted in the rat with C16 TMAC via the oral and dermal routes. In these studies, there were no organ weight changes or gross pathological / histopathological findings in the male and female reproductive organs covered by the protocol. A 90 day repeated dose oral toxicity study in the rat with the read-across substance C12-18 TMAC also showed no treatment-related organ weight, gross pathological or histopathological changes in the investigated male and female reproductive organs. Finally, developmental toxicity testing was conducted on both rat and rabbit in the read-across substance C12-16 ADBAC. No effects on developmental parameters were seen in either species at non-maternally toxic doses. Based on the above information, the conduct of a developmental toxicity study in a second species, the rat, is not considered necessary.*"

The provided information may be interpreted as an adaptation according to Annex XI, section 1.5. of the REACH Regulation, as you refer to information on pre-natal developmental toxicity in a second species (i.e. rat) generated with the read-across substance C12-16 ADBAC. However, ECHA notes that in the technical dossier, there is no study record provided for pre-natal developmental toxicity testing in rats with C12-16

ADBAC. Since the data to be read-across for pre-natal developmental toxicity in a second species is not present in the dossier, ECHA concludes that your dossier does not contain adequate and reliable documentation of the applied method and therefore, rejects your adaptation of the information requirement under Annex XI, section 1.5. of the REACH Regulation.

b. Column 2 adaptation

The information you provided could be interpreted as an attempt to adapt the information requirement according to the third indent of Annex X, Section 8.7., column 2 of the REACH Regulation.

According to the third indent of Annex X, Section 8.7., column 2 of the REACH Regulation the study does not need to be conducted if the substance is of low toxicological activity. You must demonstrate *inter alia* that:

- it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure; and
- there is no or no significant human exposure.

ECHA notes that you have not provided any toxicokinetic data to show that there is no systemic absorption of the registered substance. Moreover, in the dossier you state that the substance C12-16 ADBAC (which you use as a read-across substance for the second species prenatal developmental toxicity endpoint) is absorbed and distributed over the body, albeit in low quantities. Furthermore, the uses of the registered substance indicate that there is significant human exposure, as the substance is used by consumers (cosmetic products; furniture floor and leather care), in articles, and by professional workers.

Therefore, ECHA rejects an adaptation of the information requirement according to the third indent of Annex X, Section 8.7., column 2 of the REACH Regulation.

In conclusion, the data waiving provided to fulfill the information requirements of Annex X, Section 8.7.2., column 1 (developmental toxicity study in a second species) neither meets the specific rules for adaptation of Annex XI, Section 1.5., nor Annex X, Section 8.7., column 2 of the REACH Regulation.

In your comments on the PfA you expressed your intention to update the registration dossier to include all the missing relevant data and study results, including the pre-natal developmental toxicity study in rats with the analogue substance C12-16 ADBAC ([redacted] 1992). According to the information provided in your comments, ECHA can already note that the [redacted] study (1992) is a study conducted according to OECD TG 414 and is GLP compliant, and on this limited basis appears to be adequate and reliable. However, ECHA cannot fully assess the study as currently a robust study summary is not available in your comments or in the technical dossier. ECHA notes that the evaluation of all the new information provided in the later update(s) of the registration dossier will only be performed at the follow-up evaluation stage, pursuant to Article 42 of the REACH Regulation (after the final decision is sent out by ECHA).

As explained above, currently there is an information gap and it is necessary to provide information for this endpoint.
The test in the first species was carried out by using a non-rodent species (rabbit). According to the test method OECD 414, the rat is the preferred rodent species. On the

basis of this default assumption, ECHA considers that the test should be performed with rat as a second species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid, ECHA concludes that testing should be performed by the oral route.
Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information using the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: OECD TG 414) in a second species (rat) by the oral route.

2. Ready biodegradability (Annex VII, Section 9.2.1.1)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Pursuant to Articles 10(a)(vii) of the REACH Regulation, the information set out in Annexes VII to XI must be provided in the form of a robust study summary, if required under Annex I. Article 3(28) of the REACH Regulation defines a robust study summary as 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. Guidance on the preparation of the robust study summaries is provided in the ECHA Practical Guide 3: 'How to report robust study summaries'.

"Ready biodegradability" is a standard information requirement as laid down in Annex VII, Section 9.2.1.1. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided the following study record to fulfil the standard information requirement of Annex VII, Section 9.2.1.1.: Key study, reliability 1, [redacted] (2006), GLP compliance: yes, test method: according to OECD Guideline 301B (OECD TG 301B) with the registered substance.

You consider this study is adequate to conclude that the registered substance is readily biodegradable. However, as specified in *ECHA Guidance on Information Requirement and Chemical Safety Assessement*, Chapter R.7b, Section R.7.9.4. (Version 4.0, June 2017) and considering the identity of the registered substance (i.e. mono-constituent), the pass level of 60% theoretical carbon dioxide ($ThCO_2$ biodegradation) within 28 days may be regarded as evidence of ready biodegradability when the biodegradation screening study is conducted according to OECD TG 301B. However, this pass level for ready biodegradability has to be reached in a 10-day window within the 28-day period of the test.

ECHA notes that you have not provided sufficient information in the technical dossier to evaluate if the 10-day window criteria was fulfilled.

In addition, you have provided insufficient data to verify if the validity criteria of the selected method were fulfilled. More specifically the inorganic carbon (IC) content of the test substance suspension in the mineral medium at the beginning of the test must be less than 5% of the total carbon content (TC).

In order to allow ECHA to conduct an independent assessement of the reliability of this study, in addition to the data described above, you should provide all raw data in a tabular form and the graph of percentage degradation against time for the test and reference substances, the lag phase, degradation phase, the 10-d window and slope.

Hence, the information currently provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

In order to allow an independent assessment of the study submitted, pursuant to Article 41(1) and (3) of the REACH Regulation you are requested to provide a complete robust study summary with the above missing elements for the study.

Alternatively, if you cannot submit a complete RSS or the RSS indicates that the study is not reliable as per the criteria indicated above and/or not adequate to fulfil the information requirement, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision:

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: CO2 evolution test, OECD TG 301B) or

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: MITI test (I), OECD TG 301C) or

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Closed bottle test, OECD TG 301D) or

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Manometric respirometry test, OECD TG 301F) or

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Ready biodegradability – CO2 in sealed vessels (headspace test), OECD TG 310).

Depending on the substance profile, you may conclude on ready biodegradability, by applying the most appropriate and suitable test guideline among those listed in the ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) and in the paragraph above. The test guidelines include the description of their applicability domain.

Appendix 2: Procedural history

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 decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 16 November 2017.

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

ECHA did not receive any comments by the end of the commenting period.

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

ECHA received proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments.

ECHA referred the draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-65 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

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

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported 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 the substance tested in the new tests 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 or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.