EUROPEAN CHEMICALS AGENCY

Helsinki, 14 November 2019

Addressee: [redacted]

Decision number: CCH-D-2114489574-33-01/F
Substance name: DOCUSATE SODIUM
EC number: 209-406-4
CAS number: 577-11-7
Registration number: [redacted]
Submission number: [redacted]
Submission date: 22/11/2018
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. **High-pressure liquid chromatogram, gas chromatogram (Annex VI, Section 2.3.6.);**

2. **Description of the analytical methods (Annex VI, Section 2.3.7.);**
   - **Identification and quantification of the counter-ion**

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

You have to submit the requested information in an updated registration dossier by ***22 November 2021***. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

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 Wim De Coen, 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.

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Appendix 1: Reasons

I. SUBSTANCE IDENTITY

In accordance with Article 10(a)(ii) of the REACH Regulation, the technical dossier must contain information on the identity of the substance as specified in Annex VI, Section 2 to the REACH Regulation. In accordance with Annex VI, Section 2 the information provided has to be sufficient to enable the identification of the registered substance.

1. High-pressure liquid chromatogram, gas chromatogram (Annex VI, Section 2.3.6.)

According to Annex VI, section 2.3.6 of the REACH Regulation, the registration needs to contain a chromatogram (GC or HPLC). According to the Appendix II of the Guidance for identification and naming of substances under REACH and CLP (Version 2.1, May 2017), the information provided with the chromatogram shall include the chromatogram itself and the "Results (indicate the main peaks important for substance identification)".

The analytical data provided in the registration dossier does not contain a chromatogram together with the results summarised in a peak table.

ECHA considers that in the absence of a chromatogram, the provided analytical information is not sufficient to confirm the composition of the registered substance and thereby to fulfil the information requirement.

You need to provide analytical data that is sufficient to confirm the composition of the registered substance. The chromatogram shall be accompanied by a peak table including peak position, area, mass percent and the assignment given. You need to ensure that the information given in the dossier is consistent.

As for the reporting in the registration dossier, the information should be included in IUCLID section 1.4.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation you have agreed to provide requested information. ECHA awaits for further information to be submitted in the registration dossier by the deadline indicated in the decision. Concerning your request to prolong the decision deadline, ECHA has assessed and responded to it below.

2. Description of the analytical methods (Annex VI, Section 2.3.7.)

Annex VI, section 2.3.7 of the REACH Regulation requires that each registration dossier contains a sufficiently detailed description of the analytical method used for establishing the composition of the registered substance and therefore its identity. This information shall be sufficient to allow the method to be reproduced.

Your substance is identified as "sodium 1,4-bis[(2-ethylhexyl)oxy]-1,4-dioxobutane-2-sulfonate", however the description of the analytical methods used to identify and quantify the sodium counter-ion is missing.

Therefore, your dossier does not have sufficient information to verify the reported composition of the registered substance and therefore its identity.

Accordingly, you are required to provide the description of the analytical method used for the identification and quantification of the counter-ion (e.g. elemental analysis, etc.). The description shall be sufficient for the methods to be reproduced and shall therefore include details of the experimental protocol followed, any calculation made and the results obtained.

You shall ensure that the analytical data provided on the quantification of the substance is consistent with the composition and identity reported for the substance.

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

In your comments on the draft decision according to Article 50(1) of the REACH Regulation you have agreed to provide requested information. ECHA awaits for further information to be submitted in the registration dossier by the deadline indicated in the decision. Concerning your request to prolong the decision deadline, ECHA has assessed and responded to it below.

II. TOXICOLOGICAL INFORMATION REQUIREMENT

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.

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

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).

The technical dossier contains information on a pre-natal developmental toxicity study in rats by the oral route using the registered substance as test material. However, there is no information provided for a pre-natal developmental toxicity study in a second species.

You have sought to adapt the information requirement according to Annex IX, Section 8.7.2., column 2, which requires that "a decision on the need to perform a study at this tonnage level or the next on a second species should be based on the outcome of the first test and all other relevant available data." However, for Annex X dossiers a pre-natal developmental toxicity study in a second species is a standard information requirement and an adaptation based on Annex IX, Section 8.7.2., column 2 does not apply.

You have further stated that (1) the substance has long history of pharmaceutical and dietary uses and various safety data are generated on this substance including various repeated dose, reproductive and prenatal developmental toxicity studies, (2) the available three generation and two generation reproductive toxicity studies shows no adverse effect on reproductive or teratological effects, and (3) that testing in rabbit is not possible due to particular surfactant properties in the gastro-intestinal tract of rabbits leading to diarrhoea followed by mortality.

ECHA acknowledge the long historical use of the substance and available information on reproductive toxicity (1), however, the available information does not meet the specific

adaptation rules of Annex X, Section 8.7.3., column 2 or the general adaptation rules of Annex XI for the following reasons.

The provided pre-natal developmental toxicity studies and the two reproductive toxicity studies (2), together or separately, do not meet the information requirement of pre-natal developmental toxicity study in second species. Both pre-natal developmental toxicity and the reproduction toxicity studies are performed using the same species (rats). Furthermore, the reproductive toxicity studies do not address pre-natal developmental toxicity with sensitivity and depth of investigations (e.g. external, skeletal and visceral alterations) which would allow concluding on prenatal developmental toxicity with equal confidence than an OECD TG 414 study.

In the registration dosser you have stated, but not demonstrated, that the rabbit might not be a suitable species for testing (3). In your comments to the draft decision you outline further details of the oral repeated dose toxicity study in rabbits (Benaglia, 1943) demonstrating rabbit as an unsuitable species for testing. ECHA acknowledges your concern and agrees the study should be conducted in an appropriate second species (e.g. mouse). Robust reporting of the supporting information for species selection should be included in your dossier. Concerning your request to prolong the decision deadline, ECHA has assessed and responded to it under Appendix 2, Procedural history.

For all the reasons presented above, the information 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.

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) R.7a, chapter 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 derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: OECD TG 414) in a second species (that is appropriate) by the oral route.

Deadline to submit the requested information in this decision

The timeline indicated in the draft decision to provide the information requested is 18 months from the date of adoption of the decision.

In your comments on the draft decision, you requested an extension of the timeline to 30 months. You justified your request stating that for animal protection reasons, first elaboration on human info is considered. In addition, tolerance has to be tested in rabbits if information on human applications does not prove suitable for cross reading. The estimated turnaround time is further justified taking into account that the species may have to be changed. Therefore, you noted that the total time of at least 30 months seems most realistic.

ECHA notes that, as explained under Appendix 1, section 3, you already demonstrated rabbit as an unsuitable species for testing. Therefore sufficient time for testing is 24 months as the 9 months for testing tolerance in rabbit is not needed. ECHA has amended the deadline to 24 months.

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 2 May 2018.

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 requests and amended the deadline.

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

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

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 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.