EUROPEAN CHEMICALS AGENCY

Helsinki, 6 April 2017

Addressee: [redacted]

Decision number: TPE-D-2114355336-48-01/F
Substance name: 1-Propanaminium, N-(3-aminopropyl)-2-hydroxy-N,N-dimethyl-3-sulfo-, N-(C8-18(even numbered) acyl) derivs., hydroxides, inner salts
List number: 939-455-3
CAS number: NS
Registration number: [redacted]
Submission number: [redacted]
Submission date: 20-07-2016
Registered tonnage band: 100-1000T

## DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA has taken the following decision.

**Your testing proposal is accepted and you are requested to carry out:**

1. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats using the registered substance**
2. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rats or rabbits), oral route using the registered substance**
3. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) using the registered substance**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **15 April 2019**. You shall also 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. 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, 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.

Authorised[1] by Claudio Carlon, Head of Unit, Evaluation E2

[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**

The decision of ECHA is based on the examination of the testing proposals submitted by you for the registered substance 1-Propanaminium, N-(3-aminopropyl)-2-hydroxy-N,N-dimethyl-3-sulfo-, N-(C8-18(even numbered) acyl) derivs., hydroxides, inner salts, EC 939-455-3 or *Cocamidopropylhydroxysultaine C8-18 (CAS 68139-30-0 or CAS 70851-08-0*).

In your original submission [redacted] you intended to cover the information requirements for a sub-chronic toxicity (90-day) study (Annex IX, 8.6.2.), pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) and a long-term toxicity testing on fish (Annex IX, 9.1.6.3.). After receiving ECHA's draft decision, you have provided comments and have updated your registration on 20 July 2016 (submission number: [redacted]). Furthermore you have provided, in the technical dossier, under the endpoint specific summaries, further information on the tested material for the aquatic toxicity tests.In a proposal for amendment a Member State competent authority proposes to accept the testing proposed by you on the registered substance (C8-18) and delete the additional tests requested in the decision and instead ask for further substance identity information on the compositions particularly the similarities. In your comments on the proposal for amendment you agree to delete the additional test requests but you disagree to provide further information on the substance identity. After a re-evaluation ECHA agrees on deleting the additional requests.

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

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rodents by the oral route according to EU B.26/OECD TG 408 with the registered substance.

You proposed testing by the oral route. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA agrees that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, the substance is a liquid of very low vapour pressure and no uses with spray application are reported that could potentially lead to aerosols of inhalable size.
Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

You did not specify the species to be used for testing. According to the test method EU B.26/OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

Therefore, pursuant to Article 40(3)(a)of the REACH Regulation, you are requested to carry out the proposed study with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD TG 408).

**2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species**

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

A pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for a pre-natal developmental toxicity study according to EU B.31/OECD TG 414.

ECHA considers that the proposed study performed with the registered substance is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

You did not specify the species to be used for testing. According to the test method EU B.31/OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with rats or rabbits as a first species.

You did not specify the route for testing. 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 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in a first species (rats or rabbits), oral route (test method: EU B.31/OECD TG 414).

*Notes for your consideration*

For the selection of the appropriate species you are advised to consult ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6.2.3.2 (July 2015).

## 3. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for testing the registered substance 1-Propanaminium, N-(3-aminopropyl)-2-hydroxy-N,N-dimethyl-3-sulfo-, N-(C8-18(even numbered) acyl) derivs., hydroxides, inner salts (EC No 939-455-3) for long-term toxicity testing on Fish Juvenile Growth test, OECD TG 215 with the following justification: *"This study is proposed to fulfil the requirements for both Cocamidopropylhydroxysultaine C8-18 and C12-18 substances (distinct dossiers), using the C8-C18 as test substance."*

ECHA notes that the registered substance is a UVCB and a surfactant and therefore it is justified to study chronic effects on fish as you proposed. Furthermore, the substance has a wide range of uses with high releases to the environment, from industrial use as formulation (formulation of low viscosity liquids, e.g. shampoo, hair conditioner, shower gel, foam bath, herbal hair colorant; large scale), or at industrial sites; but also professional and consumer uses such as personal care products or washing and cleaning products; from closed to open systems. As indicated by you in your Chemical Safety Report for the uses hereby mentioned: *"Releases to the environment for these uses are the same as for all other professionnal and consumer uses."*

In addition, for some exposure scenarios (e.g. formulation of liquid detergents or maintenance products, use at industrial sites) the RCRs are close to 1 for fresh and marine water but also soil.

Therefore the long-term toxicity testing on fish is required.

In your dossier update, you now agree to perform the long-term toxicity testing according to OECD TG 210 instead of the originally proposed OECD 215 and therefore modified your testing proposal for this test guideline.

ECHA considers that for the endpoint of long-term toxicity testing on fish pursuant to Annex IX, section 9.1.6.1, the FELS toxicity test according to OECD TG 210 is the most sensitive of the standard fish tests available as it covers several life stages of the fish from the newly fertilised egg, through hatch to early stages of growth and should therefore be used (see ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R7b, Figure R.7.8-4 page 26). The test method OECD TG 210 is also the only suitable test currently available for examining the potential toxic effects of bioaccumulation (ECHA Guidance R7b, version 2.0, November 2014, p. 26). For these reasons, ECHA considers the FELS toxicity test using the test method OECD TG 210 as appropriate and suitable.

ECHA notes that there were no indications in the dossier from the short-term toxicity studies on aquatic species that fish would be substantially more sensitive than aquatic invertebrates or algae.

Therefore, pursuant to Article 40(3) (a) of the REACH Regulation, you are requested to carry out the following test using the registered substance subject to the present decision as listed above: Fish, early-life stage (FELS) toxicity test (test method: Fish, early-life stage toxicity test, OECD TG 210)

*Notes for your consideration*

You have not discussed the surface activity as a potential challenge in interpretation of the results obtained from the aquatic toxicity studies or for the selection of the test material for the testing proposal in the technical dossier.

As the substance is surface active, it is known that it can form dispersions or emulsions in which the bioavailability is difficult to ascertain, even with careful solution preparation. Moreover, the micelle formation can result in an overestimation of the bioavailable fraction even when a solution seems to be formed. This may present significant problems of interpretation. It is recommended in the ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7b: Endpoint specific guidance, Version 3.0, February 2016, that *"Toxic effect concentrations for dispersions and emulsions should be compared with the dispersibility limit (i.e., the limit at which phase separation takes place) or the critical micelle concentration (CMC) for a substance in water rather than with its water solubility limit. The bioavailable concentration does not change above the CMC, even at higher dosing levels. The highest test concentration should either be 1000 mg active ingredient/litre or the dispersibility limit/CMC, whichever is lower."* Therefore, monitoring the exposure of the test material during the experiment is needed to verify the exposure.

Finally, according to Commission Regulation (EU) 2016/266 of 7 December 2015 amending, for the purpose of its adaptation to technical progress, Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 prescribes: *"[...] If the test method is used for the testing of a MCS, UVCB or mixture, sufficient information on its composition should be made available, as far as possible, e.g. by the chemical identity of its constituents, their quantitative occurrence, and relevant properties of the constituents."* This means that you should provide sufficient information on the different constituents present in the tested material (analytical monitoring of constituents).

## Appendix 2: Procedural history

ECHA received your registration containing the testing proposal(s) for examination pursuant to Article 40(1) on 26 April 2013.

ECHA held a third party consultation for the testing proposal(s) from 18 September 2014 until 3 November 2014. ECHA did not receive information from third parties.

This decision does not take into account any updates after **20 July 2016**, 30 calendar days after the end of the commenting period.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation:

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

You updated your registration on 20 July 2016. ECHA took the information in the updated registration into account, and did not amend the draft decision. The updated information is reflected in the Reasons (Appendix 1).

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

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s).

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.

In addition, you provided comments on the draft decision. These comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5).

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-52 meeting and ECHA took the decision according to Article 51(6) of the REACH Regulation.

## Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided in your registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

2. Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

3. In carrying out the test(s) required by the present decision it is important to ensure that the particular sample of substance tested 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. If the registration of the substance covers different grades, the sample used for the new test(s) must be suitable to assess these. Furthermore, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.