ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 4 November 2016

Addressee: [redacted]

Decision number: CCH-D-2114347473-48-01/F
Substance name: Fatty acids, C16-18 (even numbered), ammonium salts
EC number: 939-066-9
CAS number: NS
Registration number: [redacted]
Submission number: [redacted]
Submission date: 01.03.2013
Registered tonnage band: 100-1000T

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. **Name or other identifier of the substance (Annex VI, Section 2.1.) of the registered substance**
   - **Chemical name;**
   - **Manufacturing process;**
2. **Description of the analytical methods (Annex VI, Section 2.3.7.) of the registered substance;**
3. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route with the registered substance;**
4. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with the registered substance;**
5. **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) with 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 **11 May 2018**. 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. 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 Ofelia Bercaru, Head of Unit, Evaluation E3

[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

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

1. Name or other identifier of the substance (Annex VI, Section 2.1.)

You have identified the registered substance as of Unknown or Variable composition, Complex reaction products or Biological materials (UVCB). Information required to be provided according to Annex VI section 2.1. of the REACH Regulation on the naming of UVCB substances such as the registered substance shall consist of two parts: (1) the chemical name and (2) a more detailed description of the manufacturing process, as indicated in chapter 4.3 of the Guidance for identification and naming of substances under REACH and CLP (Version: 1.3, February 2014) - referred to as "the Guidance" thereinafter.

The chemical name assigned by you to the registered substance is "Fatty acids, C16-18 (even numbered), ammonium salts". ECHA interprets this name as describing a substance comprising ammonium salts of carboxylic acids with saturated alkyl chain lengths C16 and C18. You indicated, in the description of the manufacturing process, that [redacted]). There was no indication that fatty acids with C16 alkyl chains were used as a starting material.

The name of the registered substance specified in the IUPAC name field of section 1.1 of your IUCLID dossier is inconsistent with the information provided for the manufacturing process description because [redacted] whilst the name of the registered substance refers also to C16 alkyl chains. Based on the description of the manufacturing process included in section 3.3 of your IUCLID dossier it is not possible to conclude how the fatty acids C16, ammonium salts are formed. ECHA therefore concludes that the manufacturing process has not been provided to a sufficient level of detail for the identification of the registered substance.

Therefore, you are requested to provide a more detailed manufacturing process description that clarifies the composition and name of your substance, particularly in terms of the origin of the C16 alkyl chains. The description needs to include all the relevant steps, the ratio of all reactants and the process parameters such as temperature and pressure.

As for the reporting of the information in IUCLID, the chemical name and manufacturing process description shall be specified in the "IUPAC name" and "Description" field in IUCLID section 1.1, respectively.

In your comments on the draft decision, you indicated that you agreed to provide the requested information.

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

Description of the analytical methods for the identification of the substance is a formal information requirement included in Annex VI Section 2.3.7. of the REACH Regulation.

The description of the chromatographic method used to quantify the substance is not included in your IUCLID registration dossier. Additionally, the ammonium counter ion identification and quantification method and the results of such analysis are not included in your IUCLID registration dossier.

ECHA regards this required information scientifically relevant for the registered substance. As the information on analytical methods is not available in the technical dossier, neither can ECHA verify the identity of the substance registered nor reproduce the methods used as stipulated by Annex VI, Section 2.3.7. of the REACH Regulation.

You are requested to submit the description of the chromatographic method used to quantify the registered substance together with the description of the method used to identify and quantify the ammonium counter ion. The descriptions shall be given in such detail that the methods can be reproduced. In the case of the ammonium counter ion analysis, typical results of the analysis also need to be reported such that the 1:1 ratio between the carboxylate and ammonium ions can be confirmed.

As for the reporting of the description of the analytical methods and their typical results in the registration dossier, the information should be included in IUCLID section 1.4.

In your comments on the draft decision, you indicated that you agreed to provide the requested information.

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "pre-natal developmental toxicity study" (test method EU B.31./OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. 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.

You have sought to adapt this information requirement according to Annex IX, Section Annex XI, Section 1.2. You have provided four studies for your Weight of Evidence approach, an OECD 422 study on docosanoic acid with Klimisch score 1, a developmental study with no guideline on octanoic acid with Klimisch score 3, a developmental study with no guideline on magnesium stearate with Klimisch score 4, a developmental study with no guideline on ammonium acetate with Klimisch score 3.

You provided the following justification for the adaptation: "*A combined repeated dose and reproduction/developmental screening was performed on docosanoic acid by the Ministry of Health, Labour and Welfare (Japan, 1998) according to OECD Guideline 422. (...) The compound did not demonstrate any adverse effects on the sex ratio, body weights or viability of pups. Also, no morphological abnormalities in pups were observed in any of the treated groups. The NOEL for maternal and reproductive toxicity was determined to be 1000 mg/kg bw/day for both males and females.*"
Additionally you describe the results of developmental studies with octanoic acid ([redacted]), magensium stearate, [redacted] and by [redacted].
You conclude: "*Taking into account the available experimental results, the weight of evidence approach was applied and the NOAEL for developmental toxicity for the substance Fatty acids, C16 -18 (even numbered), ammonium salts was determined to be 1000 mg/kg bw/day (based on the worst case assumption).*"

However, ECHA considers that your adaptation does not meet the general rule for adaptation of Annex XI, Section 1.2. ECHA firstly considers whether the individual studies meet the information requirement for Annex IX, 8.7.2.

The developmental study with no guideline on octanoic acid with Klimisch score 3 fails to cover key parameters of OECD Test Guideline 414, specifically paragraph 12: "Normally, the test substance should be administered daily from implantation (e.g., day 5 post mating) to the day prior to scheduled caesarean section." In this study, the substance was dosed one time only. Additionally, OECD TG 414 paragraph 10 states: "Groups with fewer than 16 animals with implantation sites may be inappropriate", and this study has only 10 or 12 animals per group. Consequently, there is not adequate and reliable coverage of all of the key parameters foreseen to be investigated in the corresponding test method.

The developmental study with no guideline on magnesium stearate with Klimisch score 4 used a single exposure of the animals, and the number of animals were fourteen or thirteen per group. This study therefore fails to provide coverage of all of the key parameters of the test guideline for the same reasons as set out in the octanoic acid study.

The developmental study with no guideline on ammonium acetate with Klimisch score 3 used eight (controls) or nine (ammonia groups) female animals per group, and so fails to meet the requirement for number of animals set out in OECD TG 414. Additionally, in this study, the animals were not killed before birth, and so there is no examination of foetuses for soft tissue and skeletal changes, as required in paragraphs 28-32 of OECD 414. Consequently, key parameters foreseen to be investigated in the corresponding test methods are not covered.

In the technical dossier you have provided a study record for a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD TG 422). However, this study does not provide the information required by Annex IX, Section 8.7.2. because it does not cover key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations.

On this basis, the individual studies individually fail to meet the information requirement for a pre-natal developmental toxicity study.

ECHA next considers whether there may be sufficient weight of evidence from these independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property, while the information from each single source alone is regarded insufficient to support this notion. ECHA notes that there is no consideration in your justification of why the independent sources of information fail to meet the information requirement, nor how the four pieces of information together provide a sufficient weight of evidence. ECHA accordingly considers that you have not provided adequate and reliable documentation to explain your Weight of Evidence adaptation. In the absence of a justification for why there is a sufficient weight of evidence from the independent sources of evidence, and since the individual independent sources of information are insufficient, ECHA considers that you have not met the requirement of Annex XI, 1.2 to combince multiple sources of information.

In a separate attachment in section 13, you have provided additional arguments based on QSAR Application Toolbox predictions: *"On one hand, the analogue substances ammonium, sodium and magnesium salts of fatty acids (C8-C22) and in the other hand, ammonia and its analogues...the available experimental data performed on the analogue substances confirms their analogy since similar results were obtained in the laboratory tests, demonstrating at the same time the consistency of the weight of evidence approach."* Although this adaptation makes reference to (Q)SAR, there is no adequate and reliable documentation of the QSAR method provided, as required by Annex XI, 1.3. This adaptation must also be rejected.

As explained 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.

In your comments on the draft decision, you state that *"there is not available data on the substance to cover OECD 414 information"* and that you would like *"to submit information on analogues and to use read across approach.* You state that *"There are available studies on the analogues (reliability score 2) which indicates no toxic effects for developmental toxicity."* You also intend to update the dossier by including robust summaries, data matrix and analogue approach.

You are also reminded that the decision does not take into account any updates submitted after 15 April 2016. All the new information in the later update(s) of the registration dossier will however be assessed for compliance with the REACH requirements in the follow-up evaluation pursuant to Article 42 of the REACH Regulation (after ECHA has sent the final decision).

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 assumption ECHA considers testing should be performed with rats or rabbits as a first 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 4.1, October 2015) 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: EU B.31./OECD TG 414) in a first species (rat or rabbit) by the oral route.

4. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. 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.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.5., column 2. You provided the following justification for the adaptation: "*In accordance with column 2 of REACH Annex IX, the study does not need to be conducted since the chemical safety assessment indicates the no need to investigate further the effects on aquatic organisms.*"

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.5., column 2 because the chemical safety report contains the outcome of the hazard assessment, but no exposure assessment has been carried out, i.e. the risk characterisation ratios have not been determined; hence, it cannot be claimed that the chemical safety assessment indicates there is no need to investigate further the effects on aquatic organisms. According to REACH Annex VII - 9.1.1 long-term aquatic toxicity study on Daphnia (Annex IX section 9.1.5) shall be considered if the substance is poorly water soluble. The substance has a water solublity of 0.05 mg/l, therefore long-term testing is recommended.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained 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.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 3.0, February 2016) *Daphnia magna* reproduction test (test method EU C.20. / OECD TG 211) is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5.

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: Daphnia magna reproduction test (test method: EU C.20./OECD TG 211).

In your comments on the draft decision, you state that "*All registrants agree to perform requested test although previously an expertise on the test feasibility are going to be requested. The registrants are going to ask for an opinion to three EU leading laboratories asking if the test material can be tested according to the indicated by ECHA guideline.*

Basic physical-chemical information on the substance indicates that aquatic toxicity test with analytical detection can be very difficult to perform. Several points are raised and have to be evaluated:

- *water solubility of the substance is below 0.05 mg/l. The water solubility of different fatty acids is different. According to theoretical knowledge, longer chains have lower water solubility. It is important to evaluate if both components can be detected analytically,*
- *the possibility of 3 dimensional macromolecules formation (micelles, nanofibers, etc.). At very low concentration has to be evaluated the role and influence of both constituents,*
- *surface equilibrium of the molecules and monolayer formation, the presence of ammonium head of the molecules can drive them to migrate to the surface and to form surface layers,*
- *hydrophobic effect and molecule sticking to surfaces*".

ECHA ackowledges that you intend to provide new information to fufil this information requirement either by conducting the test or alternatively by providing robust evidence as to why the test cannot be conducted.

Notes for your consideration

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4) if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. In such case, according to the integrated testing strategy, the *Daphnia* study is to be conducted first. If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.
Due to the low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

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. Adequate information on Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.), or Fish, short-term toxicity test on embryo and sac-fry stages (Annex IX, 9.1.6.2.), or Fish, juvenile growth test (Annex IX, 9.1.6.3.) needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.6., column 2. You provided the following justification for the adaptation "*In accordance with column 2 of REACH Annex IX, the study does not need to be conducted since the chemical safety assessment indicates the no need to investigate further the effects on aquatic organisms.*"

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.6., column 2 because the chemical safety report contains the outcome of the hazard assessment, but no exposure assessment has been carried out, i.e. the risk characterisation ratios have not been determined; hence, it cannot be claimed that the chemical safety assessment indicates there is no need to investigate further the effects on aquatic organisms. According to REACH Annex VIII - 9.1.3 long-term aquatic toxicity study on fish (Annex IX section 9.1.6) shall be considered if the substance is poorly water soluble. The substance has a water solublity of 0.05 mg/l, therefore long-term testing is recommended.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained 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.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 3.0, February 2016) fish early-life stage toxicity test (test method OECD TG 210), fish short-term toxicity test on embryo and sac-fry stages (test method EU C.15. / OECD TG 212) and fish juvenile growth test (test method EU C.14. / OECD TG 215) are the preferred tests to cover the standard information requirement of Annex IX, Section 9.1.6.

Regarding the long-term toxicity testing on fish pursuant to Annex IX, section 9.1.6.1, ECHA considers that 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 3.0, February 2016), Chapter R7b, Figure R.7.8-4). The test method OECD TG 210 is also the only suitable test currently available for examining the potential toxic effects of bioaccumulation (ECHA Guidance Chapter R7b, version 3.0, February 2016). For these reasons, ECHA considers the FELS toxicity test using the test method OECD TG 210 as most appropriate and suitable.

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: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

In your comments on the draft decision, you state that "*All registrants agree to perform requested test although previously an expertise on the test feasibility are going to be requested. The registrants are going to ask for an opinion to three EU leading laboratories asking if the test material can be tested according to the indicated by ECHA guideline.*

Basic physical-chemical information on the substance indicates that aquatic toxicity test with analytical detection can be very difficult to perform. Several points are raised and have to be evaluated:

- *water solubility of the substance is below 0.05 mg/l. The water solubility of different fatty acids is different. According to theoretical knowledge, longer chains have lower water solubility. It is important to evaluate if both components can be detected analytically,*
- *the possibility of 3 dimensional macromolecules formation (micelles, nanofibers, etc.). At very low concentration has to be evaluated the role and influence of both constituents,*
- *surface equilibrium of the molecules and monolayer formation, the presence of ammonium head of the molecules can drive them to migrate to the surface and to form surface layers,*
- *hydrophobic effect and molecule sticking to surfaces*".

ECHA ackowledges that you intend to provide new information to fufil this information requirement either by conducting the test or alternatively by providing robust evidence as to why the test cannot be conducted.

Notes for your consideration

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4), if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. In such case, according to the integrated testing strategy, the *Daphnia* study is to be conducted first. If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.

Due to the low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

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 7 April 2016.

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 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 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 your Member State.

3. In relation to the information required by the present decision, the sample of the substance used for the new test(s) 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 test(s) 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 test(s) must be suitable to assess these grades. Finally 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.