~~Confidential~~

Helsinki, 16 June 2021

Addressees
Registrants of JS_C12-18 ASME listed in the last Appendix of this decision

Date of submission of the dossier subject of a decision
05/10/2018

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts
EC number: 947-394-9
CAS number: NS

Decision number: Please refer to the REACH-IT message which delivered this communication (in format TPE-D-XXXXXXXXXX-XX-XX/F)

DECISION ON TESTING PROPOSAL(S)

Based on Article 40 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below in A.3 and A.4 below by ***23 June 2022***; and all other requested information listed below by ***2 January 2023***.

The requested information must be generated using the Substance unless otherwise specified.

A. Information required from the Registrants subject to Annex IX of REACH

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) by oral route, in one species (rat or rabbit);

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

3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211);

4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210).

Reasons for the request(s) are explained in the following appendix entitled "Reasons to request information required under Annex IX of REACH".

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annexes VII to IX to REACH, for registration at 100-1000 tpa.

How to comply with your information requirements

To comply with your information requirements you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

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.

Approved[1] under the authority of Christel Schilliger-Musset, Director of 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 A: Reasons to request information required under Annex IX of REACH

This decision is based on the examination of the testing proposals you submitted and on scientific information submitted by third parties.

1. Pre-natal developmental toxicity study

A pre-natal developmental toxicity (PNDT) study (OECD 414) in one species is an information requirement under Annex IX to REACH (Section 8.7.2.).

1.1. Information provided to fulfil the information requirement

You have submitted a testing proposal for a PNDT study according to OECD TG 414 by the oral route with the Substance.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Developmental toxicity. You provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

ECHA agrees that a PNDT study in a first species is necessary.

1.2. Specification of the study design

You proposed testing in the rat as a first species. You may select between the rat or the rabbit because both are preferred species under the OECD TG 414 (ECHA Guidance R.7a, Section R.7.6.2.3.2.).

You proposed testing by the oral route. ECHA agrees with your proposal because this route of administration is the most appropriate to investigate reproductive toxicity (ECHA Guidance R.7a, Section R.7.6.2.3.2.).

1.3. Outcome

Your testing proposal is accepted under Article 40(3)(a) and you are requested to conduct the test with the Substance, as specified above.

In your comments to the draft decision you agreed to perform the OECD TG 414 study, oral route in rats.

2. Sub-chronic toxicity study (90-days)

A sub-chronic toxicity study (90 day) is an information requirement under Annex IX to REACH (Section 8.6.2.).

2.1 Information provided to fulfil the information requirement

You have submitted a testing proposal for a Sub-chronic toxicity study (90 day) according to OECD TG 408 with the Substance.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Repeated dose toxicity. You provided your considerations concluding that there were no alternative methods which could be used to adapt the information

requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

ECHA received third party information concerning the testing proposal during the third party consultation.

A third party has noted that for so called "low toxicity substances" (substances which report a NOAEL of 1000 mg/kg bw/d), there is no added value for the human risk assessment if a 90-day study is performed: "*According to the Registration Dossier, a 28-day repeated dose toxicity study with the Registered Substance reports a NOAEL of 150 mg/kg bw/d; however, the effects reported in this study are limited to local gastric irritation and effects secondary to gastric irritation. There is no evidence of this study of systemic toxicity, relevant to the human risk assessment. Published analyses of toxicological data in REACH Registration Dossiers (Taylor et al, 2014; Taylor & Andrew, 2017) demonstrate that, for low toxicity substances reporting a NOAEL of 1000 mg/kg bw/d, there is no added value for the human risk assessment if a 90-day study is performed. It would appear that, in this case, a 90-day study is not scientifically justified and not in the interests of animal welfare. Taylor K, Andrew DJ & Rego L (2014)*.".

ECHA understands that the third party comments refer to the adaptation possibility under Annex IX, Section 8.6.2., column 2, fourth indent. This adaptation specifies that a sub-chronic toxicity study (90-day) does not need to be conducted if "*the substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and no evidence of toxicity in a 28-day study, particularly if such a pattern is coupled with limited human exposure*". ECHA notes that all criteria need to be met.

ECHA observes that the third party comments addressed only the criterion concerning "no evidence of toxicity". The third party did not submit information regarding the other cumulative criteria under Annex IX, Section 8.6.2., column 2, fourth indent.

Therefore, based on the information submitted by the third party the cumulative criteria listed in Annex IX, section 8.6.2., column 2, fourth indent are not met. ECHA notes that it is your responsibility to consider and justify in the registration dossier any adaptation of the information requirements in accordance with Annex IX, Section 8.6.2., column 2, fourth indent.

ECHA agrees that a 90-day study is necessary.

2.2 Specification of the study design

You proposed testing in the rat. ECHA agrees with your proposal because the rat is the preferred species according to the OECD TG 408. Therefore, the study must be conducted in the rat.

You proposed testing by the oral route. ECHA agrees with your proposal because this route of administration is appropriate to investigate systemic toxicity (ECHA Guidance R.7a, Section R.7.5.4.3.2.).

2.3 Outcome

Your testing proposal is accepted under Article 40(3)(a) and you are requested to conduct the test with the Substance, as specified above.

In your comments to the draft decision you agreed to perform the OECD TG 408 study in rats.

3. Long-term toxicity testing on aquatic invertebrates

Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

Under Article 40(3)(c) of REACH, ECHA may require a registrant to carry out one or more additional tests in case of non-compliance of the testing proposal with Annexes IX, X or XI of the REACH Regulation. The information requirement on Aquatic toxicity at Annex IX covers both long-term toxicity on invertebrates (Section 9.1.5.) and on fish (Section 9.1.6.). However, you have provided a testing proposal for long-term testing on fish only. In case of data gap for long-term toxicity testing on aquatic invertebrates, it is necessary to request this information as an additional test to ensure compliance with the endpoint.

3.1 Information provided to fulfil the information requirement

You have provided the following information:

1. an OECD TG 211 study on the Substance ([redacted] 1994)

We have assessed this information and identified the following issues:

A. Faulty test material

To comply with this information requirement, the test material in a study must be representative for the Substance (Article 10 and Recital 19 of REACH; ECHA Guidance R.4.1).

For study 1 above, you have identified the test material as "*Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts (ASMC-48)*". You have not provided compositional information on this test material including, among others, information on purity, on the relative abundance of alkyl sulphates salts *versus* alkyl methyl ester salts and on the distribution of the c-chain length of major constituents.

In the absence of adequate composition information on the test material, the identity of the test material and its impurities cannot be assessed, and you have not demonstrated that the test material is representative for the Substance. Therefore, the information provided is rejected.

B. Study 1. is unreliable

To fulfil the information requirement, a study must comply with the OECD TG 211 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

- the mean number of living offspring produced per parent animal surviving is ≥ 60 at the end of the test;
- for UVCBs, it must be demonstrated that concentrations were consistently maintained within 80-120% of the initial or mean measured values over the exposure duration based on a comparison of the mass spectral full-scan GC or HPLC chromatogram peak area;
- a continuous flow through exposure system is used if exposure concentrations cannot be maintained within 80-120% of nominal in a semi-static exposure system with a renewal frequency of 24 hours.

Your registration dossier provides an OECD TG 211 showing the following:

- the mean number of living offspring produced per control parent animal surviving at the end of the test was 48. Therefore, this study does not meet the minimum requirement for parental reproductive output of the OECD TG 211;
- the monitoring of exposure concentrations was conducted using a methylene blue active substance (MBAS) approach and quantification was conducted using UV-VIS at 654 nm. Therefore, the analytical method was non-specific and did not allow determining compositional change during the exposure period:
- you used a semi-static setup to conduct the test (the renewal rate was 48 to 72 hours). Using this experimental set-up, recoveries in test sample solutions varied widely and recoveries down to 9.3% were observed. Therefore, the test setup was not adequate to appropriately maintain exposure throughout the exposure phase.
- The recovery of the substance in the test samples was inconsistent throughout the study and ranged from 9.3% to 407.5%;

Based on the above, the validity criteria of OECD TG 211 listed above was not met. Furthermore, there are additional critical methodological deficiencies resulting in the rejection of the study results.

On this basis, the information requirement is not fulfilled.

3.2 Test selection and study specifications

The *Daphnia magna* reproduction test (test method: EU C.20/OECD TG 211) is appropriate to cover the information requirement for long-term toxicity on aquatic invertebrates (ECHA Guidance R.7.8.4.1.).

The Substance is difficult to test as it is ionisable and surface-active (surface tension: 31.9 mN/m). OECD TG 211 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 211. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

For multi-constituents/UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key components).

3.3 Outcome

Under Article 40(3)(c) of REACH, you are requested to carry out the additional test with the Substance, as specified above.

In your comments to the draft decision you agreed to perform the OECD TG 211 study.

4. Long-term toxicity testing on fish

Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

4.1 Information provided to fulfil the information requirement

You have submitted a testing proposal for a Fish, Early-Life Stage Toxicity Test (test method: OECD TG 210).

Your registration dossier does not include any information on long-term toxicity on fish.

ECHA requested your considerations for alternative methods to fulfil the information requirement for long-term toxicity on fish. You provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

ECHA agrees that an appropriate study on long-term toxicity on fish is needed.

4.2 Test selection and study specifications

The proposed Fish, Early-Life Stage Toxicity Test (test method: OECD TG 210) is appropriate to cover the information requirement for long-term toxicity on fish (ECHA Guidance R.7.8.4.1.).

OECD TG 210 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained under Appendix A.3, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.3.

4.3 Outcome

Your testing proposal is accepted under Article 40(3)(a) and you are requested to conduct the test with the Substance, as specified above.

In your comments to the draft decision you agreed to perform the OECD TG 210 study.

Appendix B: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. Test methods, GLP requirements and reporting

1. Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.
2. Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.
3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[2].

B. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

1. *Selection of the Test material(s)*
   The Test Material used to generate the new data must be selected taking into account the following:
   a) the variation in compositions reported by all members of the joint submission,
   b) the boundary composition(s) of the Substance,
   c) the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

2. *Information on the Test Material needed in the updated dossier*
   a) You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   b) The reported composition must include the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods,

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[3].

[2] https://echa.europa.eu/practical-guides
[3] https://echa.europa.eu/manuals

Appendix C: General recommendations when conducting and reporting new tests for REACH purposes

A. Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituents and, as indicated in ECHA Guidance R.11 (Section R.11.4.2.2), you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach, (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthetize its relevant constituents and/or fractions.

Appendix D: Procedure

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 10 August 2020.

ECHA held a third party consultation for the testing proposal(s) from 19 October 2020 until 3 December 2020. ECHA received information from third parties (see corresponding Appendix).

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

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

In your comments you agreed to the draft decision. ECHA took your comments into account and did not amend the requests.

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 E: List of references - ECHA Guidance[4] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[5]

RAAF - considerations on multi-constituent substances and UVCBs (RAAF UVCB, March 2017)[5]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[6]

[4] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[5] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[6] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix F: Addressees of this decision and the corresponding information requirements applicable to them

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.