~~Confidential~~

Helsinki, 20 September 2021

Addressees
Registrant(s) of JS-Sodium oleoyl glutamate as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
29/05/2018

Registered substance subject to this decision ("the Substance")
Substance name: Sodium Olivoyl Glutamate
EC number: 944-266-4
CAS number: NS

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***27 March 2023***.

The scope of this compliance check is limited to physical chemistry, environmental fate and behaviour and aquatic environment.

Requested information must be generated using the Substance unless otherwise specified.

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

1. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202)

2. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201)

3. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: OECD TG 301A/B/C/D/E/F or OECD TG 310)

Reasons for the request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendix entitled "Reasons to request information required under Annexes VII 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 Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 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, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[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 on Reasons common to several requests

1. **Assessment of your weight-of evidence adaptation under Annex XI, Section 1.2.**

You seek to adapt the following standard information requirements by applying (a) weight of evidence approaches in accordance with Annex XI, Section 1.2:

- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

ECHA has considered the scientific and regulatory validity of your weight of evidence approach in general before assessing the specific standard information requirements in the following appendices.

Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study.

Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach.

You have provided summaries in separate endpoint study records for short-term toxicity to daphnia, toxicity to algae and ready biodegradability. In those summaries you briefly present each of the sources of information, describe the results and conclude that this information can be used as WoE to predict the (eco)toxicological properties of the Substance for the above-mentioned endpoints.

Whilst these reports can be regarded as integrated summaries of the data sets, you have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/assumption that the Substance has or has not a particular dangerous property.

In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation and identified the following issues.

Your weight of evidence adaptation has deficiencies that are common to all information requirements under consideration and also deficiencies that are specific for these information requirements individually. The common deficiencies are set out here, while the specific ones are set out under the information requirement concerned in the Appendices below.

1. Reliability of the provided information with analogue substances

ECHA understands that you intend to predict the (eco)toxicological properties of the Substance for the listed above endpoints, from data obtained with analogue substances in a read-across approach as part of your weight of evidence adaptation.

Grouping of substances and read-across approach

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[2].

A. Scope of the grouping

i. Description of the grouping

For ecotoxicological properties you read-across between the following substances as source substances and the Substance as target substance:

- Aliphatic acid category"
- "Amino acid alkyl amides category"
- Sodium oleoyl glutamate

You have provided the following reasoning for the prediction of ecotoxicological properties:
- the same structural features
- similar metabolic pathways
- common levels and mode of human health related effects
- function.

ECHA understands that you base your predictions on the assumption that different compounds have similar (eco)toxicological properties as a result of structural similarity. You claim that all substances will show the same absence of or type of effects for toxicological properties.

ECHA notes the following deficiencies with regards to predictions of (eco)toxicological properties.

I. Characterisation of the group members

Annex XI, Section 1.5 of the REACH Regulation provides that "*substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of chemical similarity may be considered as group.*"

According to the ECHA Guidance, "*in identifying a category, it is important that all potential category members are described as comprehensively as possible*", because the purity profile and composition can influence the overall toxicity/properties of the potential category

[2] ECHA Guidance R.6

members.[3] Therefore, qualitative and quantitative information on the compositions of the category members should be provided to confirm the category membership.

Furthermore, the provided information for categories consisting of UVCB (Unknown or Variable composition, Complex reaction products or of Biological materials) substances needs to include qualitative compositional information of the individual constituents of the category members; as well as quantitative characterisation in the form of information on the concentration of the individual constituents of these substances; to the extent that this is measurable.[4]

You did not define the applicability domain of the category. Your read-across justification document does not contain compositional information for the members of your category. The Substance is an UVCBs with carbon chain length range C16-C22.

Therefore, the category membership cannot be confirmed.

II. Read-across hypothesis

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (read-across approach).

A read-across hypothesis needs to be provided, establishing why a prediction for a toxicological or ecotoxicological property is reliable. This hypothesis should be based on recognition of the structural similarities and differences between the source substance(s) and your Substance[5]. It should explain why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

Your read-across hypothesis is that the similarity in chemical structure and in some of the physicochemical /toxicological properties between the category members is a sufficient basis for predicting the properties of the Substance for other endpoints.

Similarity in chemical structure and similarity of some of the physicochemical/ toxicological properties does not necessarily lead to predictable or similar ecotoxicological properties. You have not provided a well-founded hypothesis to establish a reliable prediction for ecotoxicological properties, based on recognition of the structural similarities and differences between the category members.

In your comments to the initial draft decision you indicate that all existing available test data on the substances to be registered or their analogues almost never have an analytical characterisation of the test material used in the studies of interest. Therefore based on this observation and considering the rejection of ECHA as motivated in the draft decision, no literature data could be used in the REACH regulation scope. This is in contrast with the objective of promoting non-animal testing and replacement, reduction or refinement of animal testing required under REACH Regulation. You ask ECHA to clarify the balance between (1) REACH objectives of promoting non-animal testing and the subsequent replacement,

[3] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.4.1
[4] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.5.5
[5] *Guidance on information requirements and chemical safety assessment*, Chapter R.6: QSARs and grouping of chemicals.

reduction or refinement of animal testing including existing literature data and (2) the rational of its refusal, provided that the use of existing literature data is key-stone of REACH.

In your comments to the initial draft decision you indicate that existing categories are accepted even when they include a very broad spectrum of substances and that it is sufficient to refer to the performed evaluation of such existing categories, without the need to re-assess its rationale. The degree of similitude between the substance of interest and the substances already included in the categories used in the registration dossier is not less robust than the degree of similitude among the substances already included in the categories. As a result, you ask ECHA to clarify its comments on reliability of the provided information with analogue substance in view of such conflicting approaches among (1) its comments (that considers Annex XI test only) (2) the REACH requirements of Annexes VI and VII and (3) the acceptance of the existing categories outlined in the guidance.

Without compositional information on the source substances, no qualitative or quantitative comparative assessment of the compositions of the different category members can be completed. The information provided in your comments to your initial draft decision does not change this outcome.

Regarding the objectives of REACH, it is noted that the primary objective of REACH is the protection of human health and the environment. Literature data may be used but must comply with the conditions of Section 1.5 of Annex XI. As mentioned above, qualitative and quantitative information on the compositions of the category members should be provided to confirm the category membership because the purity profile and composition can influence the overall toxicity/properties of the potential category members.

In the case of OECD SIDS assessment, this assessment does not demonstrate that the category complies with Section 1.5 of Annex XI which OECD SIDS assessment do not intend to apply, in particular considering that OECD SIDS assessment is a screening exercise. In this case, you have not provided any explanation how this OECD SIDS assessment is relevant for the conditions set under Section 1.5 of Annex IX. Therefore, you have not demonstrated compliance with that REACH provision.

In your comments to your initial draft decision, you also invoke animal welfare, as a reason to avoid testing. It does not however constitute as such a valid justification to omit the standard information requirements of Annexes VII – IX or a valid adaptation to these information requirements.

In your comments to your initial draft decision, you ask "ECHA to clarify the balance between (1) REACH objectives of promoting non-animal testing and the subsequent replacement, reduction or refinement of animal testing including existing literature data and (2) the rational of its refusal, provided that the use of existing literature data is key-stone of REACH".

This balance is addressed under Article 13(1) specifies that information on intrinsic properties of substances may be generated by means other than tests, including existing data, provided that the conditions set out in Annex XI are met. These conditions are not met for the data on analogue(s) for the reasons set in this section 1.

Taken separately, your arguments on replacement, reduction or refinement of animal testing do not refer to any of the general adaptation possibilities under Annex XI. Minimisation of vertebrate animal testing is not provided for as an adaptation possibility under the general rules for adaptation set out in Annex XI. It is therefore unclear what adaptation possibility you refer to under Annex XI.

III. *Missing information to support the hypothesis*

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*".[6] The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include bridging studies to compare properties of the Substance and source substances.

ECHA understands that your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substance cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

In the technical dossier you have provided aquatic toxicity studies and ready biodegradability studies on analogue substances, as listed under the relevant information requirement section(s) A.1. – A.3. below.

However, these aquatic toxicity studies and ready biodegradability studies provided in the dossier for the analogue substances are considered as not adequate, for the reasons explained in section '*IV, Adequacy and reliability of source studies*' and under the relevant information requirements in the Appendices below.

Furthermore, in your technical dossier, you have not provided any studies on the Substance for any of the endpoints. Hence it is not possible to compare the properties of the analogue substances and the Substance.

IV. Adequacy and reliability of source studies

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across, among others should:

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);

IV-1 Test material identity

The Test Methods Regulation (EU) 440/2008, as amended by Regulation (EU) 2016/266, requires that "*if the test method is used for the testing of a [...] UVCB [...] 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*". Therefore, the unambiguous characterisation of the composition of the test material used to generate the source data is required to assess whether the test material is representative for the source substance as defined in the read-across justification document and thus relevant to the Substance.

[6] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

As explained above, there is currently no compositional information for the source substances. Furthermore, the information on the composition of the test materials of the source data provided in your dossier is limited in general to the generic name and/or category name of the test substance. It does not contain information on the chemical identity and quantitative occurrence of its constituents.

Without comprehensive reporting of all constituents present in the test material (including their identity and concentrations) and without consideration of the different alkyl carbon chain length, no qualitative or quantitative comparative assessment of the compositions of the different category members as test material and as registered substance can be completed.

Due to the above deficiency, ECHA concludes that it is not possible to assess whether the test material is representative for the source substance and thus relevant to the Substance. Therefore, the studies listed above cannot be considered as adequate for the purpose of classification and labelling and/or risk assessment.

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substance. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

2. Reliability of the QSAR information

Missing QPRF/QMRF

According to ECHA's Practical guide "How to use and report (Q)SARs", section 3.4, a QSAR Model Reporting Format (QMRF) and a QSAR Prediction Reporting Format (QPRF) are required to establish the scientific validity of the model, to verify that the Substance falls within the applicability domain of the model, and to assess the adequacy of the prediction for the purposes of classification and labelling.

For a QPRF this includes, among others:

- the model prediction(s), including the endpoint,
- a precise identification of the substance modelled,
- the relationship between the modelled substance and the defined applicability domain,
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

For a QMRF this includes, among others:

- the predicted endpoint, including information on experimental protocol and data quality for the data used to develop the model;
- an unambiguous definition of the algorithm, the descriptor(s) of the model and its applicability domain,
- an estimate of the goodness-of-fit and of the predictivity of the model, including information on training set and validation statistics.

For ecotoxicological information requirements, in your dossier assessed for the initial draft decision, you have provided estimated toxicity values for the endpoints derived via Danish (Q)SAR Database. You have provided summaries of the predictions and the outcome of the predictions.

However, in the dossier assessed for the initial draft decision you have not provided documentation establishing the scientific validity of the model for the QSAR predictions (i.e. QMRF and QPRF are not provided in the technical dossier, including identity of the compounds

used during the parameterisation of the models, defined descriptor and structural fragment domains[7]).

In your comments to the initial draft decision you have provided additional information about the Danish (Q)SAR Database predictions:

- User manual for the software for the Danish (Q)SAR Database (Annex II)
- Full report of the model for the QSAR predictions provided (Annex I) the prediction report, which includes results for all endpoints predicted and for the automatic applicability domain check ("in"/"out"))
    - Endpoint 5.2.1: ESR "Biodegradation in water: screening tests - Aliphatic acids category"
    - Endpoint 6.1.3: ESR "Short-term toxicity to aquatic invertebrates - Sodium oleoyl glutamate"
    - Endpoint 6.1.5: ESR "Toxicity to aquatic algae and cyanobacteria - Sodium oleoyl glutamate"

      In more detail specifically:
    - QSAR predictions for Aquatic toxicity endpoints (Daphnia magna 48 h and Aquatic toxicity endpoints (Pseudokirchneriella 72 h) provided in the comments:
        - DK battery approach (Battery/Leadscope/SCIQSAR). All three predictions "IN AD"
        - EPI ECOSAR results via the Danish (Q)SAR Database
    - QSAR predictions for ready biodegradability endpoint provided in the comments:
        - EPI BIOWIN results via the Danish (Q)SAR Database
        - DK battery approach (E Ultra/Leadscope/SCIQSAR)
            - Result: not biodegradable

ECHA has assessed the provided information and identified the following issues:

Information generated by application of various QSARs applied by you raises the same deficiencies irrespective of the information requirement for which it is invoked. Accordingly, ECHA addressed these deficiencies in the present Appendix, before assessing the specific standard information requirements in their specific appendices.

- Lack of or inadequate documentation of the model (QMRF), including:
- Inadequate information on the predicted endpoint, including no information on experimental protocol and data quality for the data used to develop the model
- Inadequate information on the estimate of the goodness-of-fit and of the predictivity of the model, including no information on training set and validation statistics
- Lack of or inadequate documentation of the prediction (QPRF)
- Inadequate documentation of the model prediction, including no information on the endpoint
- Inadequate documentation of close analogues, including no considerations on how predicted and experimental data for analogues support the prediction

In your comments to the initial draft decision, you provided additional information about the Danish QSAR Database predictions; the user manual for the software (Annex II) and perhaps instead of the link to the Danish QSAR Database, you provided the prediction report which includes results for all endpoints predicted and for the automatic applicability domain check ("in"/"out")(Annex I)).

[7] ECHA Guidance R.6, Section R.6.1.10 32 ECHA Guidance R.6, Section R.6.1.5

However, based on issues concerning adequacy (input structure) and documentation (based on the provided documentation), you have not demonstrated the validity and reliability of the predictions.

You have not provided the details to assess the adequacy and validity of the prediction:

The reliability and adequacy of the predictions cannot be established.

So this information does not change the outcome of ECHA's assessment.

Applicability domain

Under ECHA Guidance R.6.1.5.3., a substance must fall within the applicability domain specified by the model developer.

You state that the Danish QSAR Database considers that the main consistuent used as a prepresentative part of the Substance falls within the applicability domain of the model. However, neither the software nor you provide sufficient information to confirm this claim. Predictions from Danish QSAR database are provided online with limited information about the prediction (only the numerical result and IN/OUT domain, without further reasoning). Information as such is not sufficient to assess the adequacy of the prediction.

You have not provided the details to assess the adequacy and validity of the prediction:

- You did not report the results adequately to show that the applicability domain criteria was fulfilled for each of the models.

The reliability and adequacy of the predictions cannot be established.

So this information does not change the outcome of ECHA's assessment.

Adequacy of the prediction

Under ECHA Guidance R.6.1.7.3. a prediction is adequate for the purpose of classification and labelling and/or risk assessment if the following condition is met:

- representative structure(s) for the assessment are selected.

In your comments to the initial draft decision, you outline that sodium olivoyl glutamate is an UVCB substance, in which the main constituent is sodium oleoyl glutamate [redacted], that represents the preponderant carbon chain in the substance. Therefore, you consider that QSAR predictions were provided for a substance that fully represents the Substance under registration.

Although sodium oleoyl glutamate is identified as the main constituent of the Substance [redacted] no substantiation of your statement on representative of the preponderant carbon chain in the Substance is provided nor justification how the carbon range would impact the toxicity assessment. There are other constituents, present in the Substance. However, there is no structural information given on these. No justification how the carbon range would impact the toxicity assessment. The information on the substance identity and the justification for the selection of the representative structure is not adequate for the purpose of classification and labelling and/or risk assessment.

So this information does not change the outcome of ECHA's assessment.

Therefore, the QSAR predictions are not considered reliable, because it cannot be established whether the (Q)SAR models are scientifically valid and/or that the Substance falls within the applicability domain of the prediction models.

Unexplained use of an analogue substance for prediction

In addition, the predictions were provided for an analogue substance sodium oleoyl glutamate, not for the Substance itself. However, as already explained in the section above, your read-across adaptation under Annex XI, Section 1.5. is rejected.

In your comments to the initial draft decision you indicate that you consider that the QSAR predictions were provided for a substance that fully represents the Substance under registration. Your comments have been addressed above.

In your comments to the initial draft decision you indicate that existing categories are accepted even when they include a very broad spectrum of substances and that it is sufficient to refer to the performed evaluation of such existing categories, without the need to re-assess its rationale. The degree of similitude between the substance of interest and the substances already included in the categories used in the registration dossier is not less robust than the degree of similitude among the substances already included in the categories. As a result, you ask ECHA to clarify its comments on reliability of the provided information with analogue substance in view of such conflicting approaches among (1) its comments (that consider Annex XI test only) (2) the REACH requirements of Annexes VI and VII and (3) the acceptance of the existing categories outlined in the guidance.

As indicated in your comments, guidance R6 QSARs states that "If the chemical is a member of a category that has already been evaluated, its inclusion into the new category should be justified". There is no automatic acceptance of 'existing categories'; they must comply with the REACH Regulation. As stated above your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected and you have not addressed the reliability issues identified for the QSAR information.

The adaptation you provided does not fulfil the criteria specified in Annex XI, Section 1.3. and it is therefore rejected.

Additional issues related to weight of evidence are addressed under the corresponding endpoints.

Appendix A: Reasons to request information required under Annex VII of REACH

1. Short-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

You have adapted the standard information requirements mentioned above according to Annex XI, Section 1.2. (weight of evidence).

You have provided the following sources of information to support your adaptations;

i. Supporting study: Read-across OECD SIDS ALIPHATIC ACIDS CATEGORY (2014)
ii. Weight-of–evidence : QSAR (2018) on analogue substance Sodium oleoyl glutamate (CAS Nr. 35057-11-5)
iii. Weight-of–evidence: Read-across based on grouping of substances (category approach)

We have assessed this information and identified the following issues:

Weight of evidence

As explained in Section 1 of the Appendix common to several requests, the weight of evidence must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

To fulfil the information requirement, normally a study according to OECD TG 202 must be provided. The key element investigated by this test is immobilisation of aquatic invertebrate. The sources of information (i) and (ii) provide relevant information on concentrations of test material leading to a 50% immobilisation of daphnids. Therefore, they provide information that would contribute to the conclusion on this key element.

However, the reliability of these sources of information is significantly affected by the deficiencies identified in Section 1 of the Appendix on Reasons common to several requests.

- *Analogue study*

In addition, the reliability of the sources of information (i) is also affected by the following additional issues.

The conditions of exposure in OECD TG 202 specifies that (among others):

- the percentage of immobilised daphnids is ≤ 10% at the end of the test in the controls (including the solvent control, if applicable);
- the dissolved oxygen concentration is ≥ 3 mg/L in all test vessels at the end of the test;
- Daphnia magna (or other suitable Daphnia species) is used as test species.

In the dossier assessed for the initial draft decision, the supporting study (source i.), you provide "Table 18. Summary of Aquatic Effects", listing LC50, EC50 and ECOSAR predictions of various analogue substances belonging to the 'aliphatic acids category'. However, none of the data listed there include information on the parameters and validity criteria of the OECD TG 202. In addition, for majority of the source substances, the test organism information is not provided.

First, in your comments to the initial draft decision you indicate you have provided an Annex

3, the full OECD report from which short-term toxicity testing on aquatic invertebrates data were derived, with (i) the identification of the substances (p. 2-10) and (ii) available data on OECD TG 202 studies. Data used in the OECD document were considered as reliable by you according to the reasoning commented in Paragraph "3. Weight of evidence (WoE) approach", even if, as discusses above, in the literature data it is not possible to have a level of detail on (i) test material identity, (ii) study design, and (iii) test organism (except the name of the organism). Therefore, you asks ECHA to have the possibility to ameliorate the dossier content with a more comprehensive data reporting, without performing further testing.

The information in your comments is not sufficient for ECHA to make an assessment for the reasons provided below.

Further, you have provided not further information on the issues identified above, only comments why such information should be sufficient. For these arguments, ECHA refers to Section 1.1.A.i.II of the Appendix on reasons common to several requests.

Therefore, information provided in your comments does not change the outcome of ECHA's assessment.

Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation").

Second, in your submitted information you provide an Aliphatic acid category", SIDS Initial Assessment ReportForCoCAM 6. on pages 103 – 105, you outline the available information on the category and you include table "Table 18. Summary of Aquatic Effects". However, as indicated above for your assessment of the dossier, none of the data listed includes information on the parameters and validity criteria as per the OECD TG 202. In addition, for majority of the source substances, the test organism information is not provided.

Regarding the intent to provide future data, it should be noted that ECHA cannot take into account future data for the purpose of assessing compliance of the registration dossier with REACH.

Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation)."

Third, in your comments to the initial draft decision, you indicate that Annex VII endpoints REACH Regulation never provides that existing data shall comply with TG requirements, TG requirements are not mentioned in Annex VII column 1. It is not mandatory that literature data comply with TG requirements, otherwise most of the literature data should be disregarded. Under Annex XI general rules for adaptation Environmental properties from experiments not carried out according to GLP or not carried out according to the test methods referred to in Article 13(3), this data shall be considered to be equivalent to data generated by the corresponding test methods when they are adequate for the purpose of risk assessment.

All data provided in support for an adaptation must fulfil the conditions set by REACH for such an adaptation.

A weight of evidence is intended to adapt such study. But note that, according to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based

on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study. In order to do this, you need to know your information and be able to apply a value on it, against a known standard(s). You have not provided such assessment taking into account the reliability issues identified above.

So the information provided in your comments does not change the outcome of ECHA's assessment.

- *(Q)SAR*

In your comments to the initial draft decision, the provided QSAR documentation has been addressed in the Appendix on reasons common to several requests, under the section on the Reliability of the QSAR information Section 2 under Assessment of your weight-of evidence adaptation under Annex XI, Section 1.2., and rejected.

So this information does not change the outcome of ECHA's assessment.

We also note that the predictions (for Daphnia) from the models in the Danish battery and those from ECOSAR differ significantly. However, you have not addressed these differences and how the prediction on either would still be valid as part of a weight of evidence and the validity of respective predictions could not be assessed.

Therefore the provided supporting studies cannot be considered a reliable source of information.

- *Conclusion*

Taken together, even if sources of information i. and ii. provide information on the key element, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Accordingly, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 202 study.

Therefore, your adaptations are rejected and the information requirement is not fulfilled.

Study design

The Substance is difficult to test due to the surface active properties of the Substance (You indicated in the dossier that the technical function of the Substance during the formulation and use is surfactant; further, based on the structure of the Substance, surface activity is expected, because the Substance has hydrophilic and lipophilic moieties). OECD TG 202 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 202. 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.

2. Growth inhibition study aquatic plants

Growth inhibition study aquatic plants is a standard information requirement in Annex VII to REACH (Section 9.1.2).

You have adapted the standard information requirements mentioned above according to Annex XI, Section 1.2. (weight of evidence).

You have provided the following sources of information to support your adaptations;

i. Supporting study: Read-across OECD SIDS ALIPHATIC ACIDS CATEGORY (2014)
ii. Weight-of–evidence: QSAR (2018) on analogue substance Sodium oleoyl glutamate (CAS Nr. 35057-11-5)
iii. Weight-of–evidence: Read-across based on grouping of substances (category approach)

We have assessed this information and identified the following issues:

Weight of evidence

As explained under Appendix on Reasons common to several requests, the weight of evidence must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

To fulfil the information requirement, normally a study according to OECD TG 201, and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test, must be provided. The key element investigated by this test is growth rate of algae and, the following information must be provided:

- the concentrations of the test material leading to a 50 % and 0% (or 10%) inhibition of growth at the end of the test are estimated.

The sources of information (i) and (ii) provide relevant information on concentrations of test material leading to a 50% and 0% (or 10%) inhibition of algae growth.

However, the reliability of these sources of information is significantly affected by the deficiency identified and explained under Appendix on Reasons common to several requests. In addition, the reliability of the sources of information (i) is also affected by the following additional issues.

The conditions of exposure in OECD TG 201 specify that:

- exponential growth in the control cultures is observed over the entire duration of the test;
- at least 16-fold increase in biomass is observed in the control cultures by the end of the test;
- the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%;
- the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures is ≤ 7% in tests with Pseudokirchneriella subcapitata. For other less frequently tested species, the value is ≤ 10%;

In the endpoint study record, you indicated that the validity criteria were fulfilled. However, no information are provided on the validity criteria of OECD TG 201 outlined above. In addition, no information on the test material identity, study design, test organism (except the name of the organism) is available.

Therefore, without these critical information study (i) cannot be considered as reliable.

Taken together, even if these sources of information provide information on the key parameters, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

In your comments to the initial draft decision, the provided QSAR documentation has been addressed in the Appendix on reasons common to several requests, under the section on the Reliability of the QSAR information Section 2 under Assessment of your weight-of evidence adaptation under Annex XI, Section 1.2., and rejected.

So this information does not change the outcome of ECHA's assessment.

Accordingly, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 201 study.

Therefore, your adaptations are rejected and the information requirement is not fulfilled.

Study design

OECD TG 201 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above in A.1., the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Section A.1.

3. Ready biodegradability

Ready biodegradability is an information requirement under Annex VII to REACH (Section 9.2.1.1.).

You have adapted the standard information requirements mentioned above according to Annex XI, Section 1.2. (weight of evidence).

You have provided the following sources of information to support your adaptations;

i. Weight-of-evidence: OECD SIDS ALIPHATIC ACIDS CATEGORY (2014), containing a table with data on the aliphatic acids category members.
ii. Weight-of–evidence: Read-across based on grouping of substances (category approach)

We have assessed this information and identified the following issues:

Weight of evidence

As explained in Section 1 of the Appendix common to several requests, the weight of evidence must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

To fulfil the information requirement, normally a study according to OECD TG 301/310 must be provided. The key element investigated by this test is ultimate aerobic biodegradation.

In the source of information (i), you provided biodegradation at 28 days of various analogue substances belonging to "aliphatic acid category" in tabular form. Therefore, they provide information that would contribute to the conclusion on this key element.

However, the reliability of these sources of information is significantly affected by the deficiencies identified in Section 1 of the Appendix on Reasons common to several requests.

In addition, the reliability of the sources of information is also affected by the following additional issues.

- *Study deficiencies*

The conditions of exposure in OECD TG 301/310 specify that (among others):

- The test material identity is provided, including information on purity, presence of impurities and compositional information (if applicable);
- A reference substance (e.g. aniline, sodium benzoate, ethylene glycol or 1-octanol) of known biodegradability is tested in parallel. Biodegradation of these substances is ≥ 60% ThIC within 14 days;
- The mean amount of TIC present in the blank controls at the end of the test is ≤ 3mg C/L;
- The inoculum originates from one of the following sources: activated sludge, sewage effluents, surface waters, soils or a mixture of these;
- If activated sludge or a secondary effluent is used, it is taken from a treatment plant or laboratory-scale unit receiving predominantly domestic sewage;
- The inoculum is not be pre-adapted to the test substance;

In the study record (i), none of the reported studies listed in the table fulfil the requirements outlined above.

Therefore, the provided study (i) cannot be considered a reliable source of information.

- *QSAR*

First, your comments to the initial draft decision have been addressed in the Appendix on reasons common to several requests, under the section on the Reliability of the QSAR information Section 2 under Assessment of your weight-of evidence adaptation under Annex XI, Section 1.2..

In addition, more specifically, ECHA notes the following for EPI BIOWIN results via the Danish QSAR DB:

- There was no assessment of the applicability domain for the provided BIOWIN model.
- By running the model with the input provided by you it showed that BIOWIN 3 model is based on a training set with substances having only 1 instance of the fragment aliphatic acid, while the predicted structure has two.
    - In BIOWIN, it stated that "Currently there is no universally accepted definition of model domain. However, users may wish to consider the possibility that biodegradability estimates are less accurate for compounds outside the MW range of the training set compounds, and/or that have more instances of a given fragment than the maximum for all training set compounds." Hence you have not demonstrated that the constituent is within the BIOWIN 3 domain.

Second, regarding the Danish battery model, it has been addressed on the Reliability of the QSAR information Section 2 under Assessment of your weight-of evidence adaptation under Annex XI, Section 1.2.

- *Conclusion*

Taken together, even if these sources of information provide information on the key element, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Accordingly, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 301/310 study.

Therefore, your adaptations are rejected and the information requirement is not fulfilled.

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[8].

B. Test material

1. Selection of the Test material(s)

   The Test Material used to generate the new data must be selected taking into account the following:
   - the boundary composition(s) of the Substance,
   - 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
   - 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.
   - The reported composition must identify all the constituents as far as possible as well as their concentration (OECD GLP (ENV/MC/CHEM(98)16) and EU Tests Methods Regulation (EU) 440/2008 (Note, Annex). Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods. The reported composition must also include other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[9].

[8] https://echa.europa.eu/practical-guides
[9] 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 synthesize its relevant constituents and/or fractions.

Appendix D: Procedure

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

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

The compliance check was initiated on 9 April 2020.

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) but amended the deadline.

> The timeline indicated in the initial draft decision to provide the information requested is 12 months from the date of adoption of the decision.
>
> In your comments on the initial draft decision, you requested an extension of the timeline to 18 months. You justified your request with the following arguments, which ECHA has evaluated in turn further below:
>
> *Because of the surfactant nature of the substance, with experimental difficulties recognized by ECHA, in case the Addressee requests will not accepted by ECHA, a longer timing for performing tests is requested, with a proposed timing of 18 months.*
>
> Due to foreseen substance specific technical issues, you have requested an extension. ECHA has considered your argument and has granted the request and set the deadline to 18 months.

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[10] 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)[11]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)
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[12]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

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

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 their corresponding information requirements

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.