EUROPEAN CHEMICALS AGENCY

Helsinki, 26 March 2020

Addressee: [redacted]

Decision number: CCH-D-2114502210-75-01/F
Substance name: Disodium C-isodecyl sulphonatosuccinate
EC number: 253-452-8
CAS number: 37294-49-8
Registration number: [redacted]
Submission number: [redacted]
Submission date: 20/11/2018
Registered tonnage band: 10-100 tpa

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.);**
   - **Substance type and manufacturing process description**
2. **Description of the analytical methods (Annex VI, Section 2.3.7.);**
   - **Identification and quantification of the impurities**
3. **Composition of the substance (Annex VI, Section 2.3.);**
4. **In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.) with the registered substance;**
5. **In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.) with the registered substance.**

You have to submit the requested information in an updated registration dossier by ***2 April 2021.*** 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 and advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

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 1: Reasons

Your registration dossier contains for multiple endpoints adaptation arguments in the form of a grouping and read-across approach according to Annex XI, 1.5. of the REACH Regulation. ECHA has assessed first the scientific and regulatory validity of your Grouping and read-across approach in general before the individual endpoints.

0. Grouping and read-across approach for toxicological information

Your registration dossier contains adaptation arguments which are based on a grouping and read-across approach in accordance with Annex XI, Section 1.5. of the REACH Regulation. You have grouped registered substances and formed a group (category) of 'mono-ester sulphosuccinates' to predict from data for reference substance(s) missing toxicological properties for other substances within this group (read-across approach). You seek to adapt the information requirements for the following standard information requirements by grouping substances in the category and applying a read-across approach in accordance with Annex XI, Section 1.5:

- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.);
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.);

ECHA has considered the scientific and regulatory validity of your grouping and read-across approach in general before assessing the individual properties in this appendix.

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 category. Secondly, it is required that the relevant properties of a substance within the category may be predicted from data for reference substance(s) within this category (read-across approach). ECHA considers that the generation of information by such alternative means should offer equivalence to the information generated by prescribed tests or test methods.

Based on the above, a grouping and read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a specific toxicological property is reliable and should be based on recognition of the structural similarities and differences between the source and registered substances. This hypothesis explains why the differences in the chemical structures should not influence the toxicological properties or should do so in a regular pattern. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures. There may be several lines of supporting evidence used to justify the grouping and read-across hypothesis, with the aim of strengthening the case.

Due to the different nature of each endpoint and consequent difference in scientific considerations (e.g. key parameters, biological targets), a read-across must be specific to the endpoint or property under consideration. Key physicochemical properties may determine the fate of a compound, its partitioning into a specific phase or compartment and largely influence the availability of compounds to organisms, e.g. in bioaccumulation and toxicity tests. Similarly, biotic and abiotic degradation may alter the fate and bioavailability of compounds as well as be themselves hazardous, bioaccumulative and/or persistent. Thus, physicochemical and degradation properties influence the human health and environmental properties of a substance and should be considered in read-across assessments. However,

the information on physicochemical and degradation properties is only a part of the read-across hypothesis, and it is necessary to provide additional justification which is specific to the endpoint or property under consideration.

The ECHA Read-across assessment framework[2,3] foresees that there are two options which may form the basis of the read-across hypothesis- (1) (Bio)transformation to common compound(s)- the read-across hypothesis is that different substances give rise to (the same) common compounds to which the organism is exposed and (2) Different compounds have the same type of effect(s)- the read-across hypothesis is that the organism is exposed to different compounds which have similar toxicological and fate properties as a result of structural similarity (and not as a result of exposure to common compounds).

Finally, Annex XI, Section 1.5. lists several additional requirements, which deal with the quality of the studies which are to be read-across.

0.1. Scope of the category

You have provided two read-across documents in Section 13 of IUCLID. In the first document [redacted] the 'sulfosuccinates' are divided into five sub-categories. The second document [redacted] is a detailed read-across argumentation for the sub-category 'mono-ester sulfosuccinates'.

You have identified the following substances as 'mono-ester sulfosuccinates' category members:

1. butanedioic acid, sulfo-, mono (c16-18 and c18-unsatd. alkyl) esters, ammonium sodium salts (CAS No 147993-66-6; EC No 604-617-1);
2. disodium isodecyl sulfosuccinate (CAS No 37294-49-8; EC No 253-452-8);
3. 90268-37-4 butanedioic acid, sulfo-, 4-c12-14 (even numbered)-alkyl esters, disodium salts (CAS No 90268-37-4; EC No 939-638-8);
4. 1141 sulfosuccinat, i-c10, di-na-salz (CAS No 90268-39-3; EC No 944-611-9); and
5. 90268-36-3_master_butanedioic acid, sulfo-, 1-c12-18-alkyl esters, disodium salts (CAS No 90268-36-3; EC No 290-836-4).

These substances are hereafter indicated as substances [1] to [5].

With regard to the proposed grouping ECHA has the following observations:

0.1.1. Applicability domain of the category

As stated above, a group or category needs to defined in such a manner, based on chemical similarity, that the boundaries of the group are clearly indicated, which is referred here to as Applicability domain of the category. The applicability domain of a category is defined by the set of inclusion and/or exclusion criteria that identify the range of values within which reliable predictions can be made for category members.

Wide structural variation

In your read-across justification document, the applicability domain of your category is defined by the basic structure of the category members as "*All members of the*

[2] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

[3] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: https://echa.europa.eu/publications/technical-scientific-reports

mono-ester Sulfosuccinate subgroup, are mono-esters of sulfosuccinates. Beside the sulfosuccinate group they do not contain other bonds than C-C and C-H. The rests may be linear or branched. The regular variation of the C-chain length leads to small but systematic changes of physicochemical properties which are essential for the bioavailability which is a prerequisite for potential toxicological interactions." Furthermore you have indicated that *"The subgroup comprises different sulfosuccinates (monoconstituents and UVCBs substances) varying in C-chain length (C10-C18)"*

Based on this information, ECHA understands that the length and the linear, or branched nature of the carbon chain constitute the main structural differences among the members of your category. The range of the linear carbon chain length allowed within the category is well defined, ranging from C10 to C18, and the only cations applicable for the category members are sodium and ammonium.

Thus, concerning the chemical similarity of the members of the category, ECHA notes that one member of the category, (CAS No 147993-66-6; EC No 604-617-1) includes ammonium, which makes that substance structurally different from the other category members and is likely to have an effect on the toxicity of that substance.

Furthermore, ECHA observes that you have not provided inclusion and exclusion criteria defining the allowed structural and positioning variations in relation with the **branching** of the structure of the category members. In particular, no information on the distribution of the carbon chain length between the linear and the branched alkyl rests, i.e. the carbon chain length of the linear and the carbon chain length and positioning of the alkyl branching alkyl rests, is provided apart from referring to an overall range of C10 to C18.

In conclusion, ECHA notes that you have not addressed the variation induced by branching of the structure of substances, and that you have included a category member that contains ammonium. Therefore, ECHA considers that you have failed to adequately characterise the boundaries and the applicability domain of the category. Therefore, the range of substances for which the properties can be predicted within this category cannot be determined. Refined inclusion and exclusion criteria addressing these aspect are necessary to unambiguously establish the boundaries of the applicability domain of your category.

One source substance is not a member of the Monoester category

You have suggested that for reproductive toxicity, and pre-natal developmental toxicity one source substance for the read-across is CAS No 577-11-7, which is not a member of the category of mono-esters, as you have defined it in "applicability domain" of the justification document.

You have not provided a justification on the selection of this substance as a source substance, apart from a claim that based on "toxicological similarity between subgroups, read-across was also performed between the subgroups (e.g. between the monoester and the di-ester subgroup)". ECHA notes that the similarity between the sub-groups has not been demonstrated. Furthermore, no details on the structure or other toxic properties of this substance were included.

ECHA concludes that because there is a wide structural variation among the member of the category, you have not demonstrated that these substances are chemically similar. Furthermore, by inclusion of a substance, which is not a member of the category of

monoesters, you have contradicted with the boundaries of the applicability domain and the inclusion criteria, as you have defined them.

In your comments to the draft decision, you indicated that you intend to provide more detailed information on the read-across and further justification of the read-across on the aspects raised above.

0.1.2. Characterisation of the composition of the category members

The characterisation of the substances identified as members of a category needs to be as detailed as possible in order to confirm category membership and to assess whether the attempted predictions are not compromised by the composition and/or impurities. The information provided on the substance characterisation of the category members must establish a clear picture of the chemical structures of the constituents of the members of the category. It is recommended to follow the ECHA *Guidance for identification and naming of substances under REACH and CLP* for all source substances within the category.[4].

Branching

You indicated that the members of this category differ based on the "*The variation of the C-chain length / alkyl –group*". ECHA understands from this information that quantitative and qualitative differences with regard to the alkyl chains exist in the composition of the members of this category. You have provided, for each category member, information on the amount of one alcohol of defined carbon chain length used in the respective manufacturing process.

However, no other quantitative and qualitative information detailing the branched nature (or branching) of the specific alcohol is provided in the read-across justification document.

Since branching of the molecules may effect on toxicity of the substance, ECHA notes that you have failed to explain why different branching of the structure of some category members (or their constituents) would not compromise the attempted prediction of the toxic properties of the target substances within the category.

UVCB nature of the substances

Four of the five members of the category are UVCB substances. Considering the wide ranges of constituents in the UVCBs, their composition varies widely. You have not explained whether and how the highly variable composition may affect the toxicity of the category members, including the analogue substance, EC No 290-836-4, CAS No 90268-36-3. Therefore, ECHA considers that you have not demonstrated that the composition of the substances within the category is sufficiently similar to allow prediction of the toxicity of the target substance(s) of the category.

In conclusion, because of branching of the substances, and UVCB nature of four members of the category, ECHA considers that the level of information provided on the composition of the category members and the information provided on the composition of the substances are not adequate to establish the similarity of these substances.

Consequently, ECHA notes that you have not demonstrated that the attempted predictions of the toxicity are not compromised by the varying composition of the category members.

[4] Guidance for identification and naming of substances under REACH and CLP (version 2.1, May 2017). ECHA, Helsinki. 127 pp. Available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

In your comments to the draft decision, you indicated that you intend to provide more detailed information on the read-across and further justification of the read-across on the aspects raised above.

0.2. Predictions within the category

0.2.1. Description of your predictions of toxicological properties

In Annex XI, Section 1.5., it is provided that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group by interpolation. Therefore, the data matrix that specifies the available data should be prepared that includes the available toxicological data of the reference substance(s). Furthermore, you shoud indicate the method of prediction within the category, i.e. you should explain how the data that is available of the category members can be used to predict the toxicity of the category member(s) that lack that toxicity data. The "hypothesis", which the prediction is based on, may be e.g. that the category members share similar toxic property(ies) or that there is a trend within the category and the a given member of a category can be placed orderly (with)in this trend.

Your read-across justification document for the proposed 'mono-ester sulfosuccinates' category [redacted] covers:

- compositional information;
- the reasoning for the grouping based on structural similarity;
- information to support the read-across approach based on physico-chemical properties;
- data matrixes showing the available physico-chemical, environmental fate and (eco)toxicological data and how the data is to be read-across within the category.

You use the following arguments to support the prediction of properties within the category:
"*The subgroup [...] is built on the following characteristics:*
- similarities in the chemical process
- similar functional groups
- similar general composition [...]
The assumption that the properties of the subgroup members are similar can be shown in a first comparison of the physical-chemical and toxicological data."

You have provided the following hypothesis for the prediction of toxicological properties "*irrespective of chain length, logKow and water solubility, toxicological properties are similar between subgroup members*".

In order to support your hypothesis, you further refer to similarities in the acute toxicity, skin irritation, eye irritation, and skin sensitisation properties of the category members. You also point at the outcome of bacterial mutagenicity assays and sub-acute and sub-chronic repeated dose toxicity studies conducted with the category members.

ECHA understands that on the basis of structural similarity and similarity or regular pattern in toxicological properties for some members of the category, you consider it possible to predict the human health and environmental toxicity properties of the registered substance from the other members of the proposed 'mono-ester sulfosuccinates' category. As an integral part of this prediction, you propose that the source and registered substances have properties that are similar. ECHA considers that this information is your read-across hypothesis.

0.2.2. ECHA analysis of your predictions of toxicological properties in light of the

requirements of Annex XI, Section 1.5

ECHA has evaluated your read-across hypothesis and considered whether the justification you have provided to support your hypothesis are relevant and adequate to allow prediction of toxicological properties for the endpoints under consideration. In this regard, a number of deficiencies are identified in your justification used to support the read-across hypothesis and these are listed below.

Inconsistent results of the studies

Annex XI, Section 1.5 of the REACH Regulation requires that "*Substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as a group*". According to the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.6.2, Section R.6.2.2.2, (version 1.0, May 2008) "*a demonstration of consistent trends (*or similarity*) in the behaviour of a group of chemicals is one of the desirable attributes of a chemical category and one of the indicators that a common mechanism for all chemicals is involved*"

Consequently, it is expected that you provide a category hypothesis, which explains why and how the unknown toxicity of the target substances can be predicted using the toxicity and other data on the sources substance(s) within the category. The data that you provide for the members of the category has to support and demonstrate the validity of your hypothesis.

Repeated dose toxicity

ECHA considers that your read-across hypothesis is based upon **similarity** in physico-chemical properties and the observation of "*irrespective of chain length, logKow and water solubility, toxicological properties are similar between subgroup members*". With this consideration, you have used read-across to predict properties of category members for the endpoints genotoxicity, repeated dose toxicity, reproductive toxicity, and developmental toxicity.

To support the read-across for repeated dose toxicity and pre-natal developmental toxicity, you have submitted the oral screening test, with rats (OECD 422) made with one member of the category [5] resulting in the NOAEL of 60 mg/kg bw/day. However, the NOAEL of the 90-day oral study with the substance subject to the present decision [2] was 750 mg/kg bw/day in rats. ECHA notes that the results of these two studies suggest that there is a difference in toxicity between these substances.

In your comments to the draft decision, you indicated that the NOAEL of 60 mg/kg bw/day in the OECD 422 study (2013) with read across substance CAS 90268-36-3 is based on oral gavage dosing. TheNOAEL in the 90 day study (1975) is reported to be 174 mg/kg, based on a 0.25% dietary application. Although the NOAEL is still higher in the 90-day study, the conditions of both studies were considered to be different, therefore this is not considered as a difference in toxicity. You agree that further investigation is needed. Route is only one of the variables between these two studies and you have not ruled out the possibility that there are other reasons to the toxicity difference ECHA acknowledges your agreement that further investigations is needed.

Observation that indicates different toxicity was also made in a 14-day range finding studies performed with these two members of the category, i.e. [5] and [2], by the same laboratory in 2013. In these studies the NOAEL values were the same, but

significantly more severe effects (e.g. mortality) were noticed with [5]. These findings are further supported by the LD50-values of the two substances, i.e. 580 mg/kg bw for [5] and 2340 mg/kg for [2].

In your comments to the draft decision, you indicated that CAS 90268-36-3 indeed provides lowest LD50 of 580 mg/kg, however CAS 37294- 49-8 also reports an LD50 between 300 and 2000 mg/kg bw compared to LD50>2000 mg/kg for CAS 147993-66-6. Probably there is a slightly higher toxicity profile at the lower end of the Mono-ester category, which might be based on lower molecular weight fractions. The NOAEL of 60 mg/kg bw/day was used as a worst case NOAEL for the category. ECHA agrees that you can in principle apply a worst case approach in your predition based on read-across. However, currently there are limited information on the higher human health studies to demonstrate that the specified substances represent a worst case within the category.

ECHA concludes that your read-across justification which is based on 'similarity' among in the category members, is not supported, as there is evidence of different toxicity between two members of the category, i.e. the substance subject to the present decision [2] and source substance [5]. Consequently, you have not demonstrated the validity of your hypothesis.

In your comments to the draft decision, you indicated that the wording on similarity among category member may need to be adapted, and additional testing will be discussed under the Substance specific section. ECHA takes note of your intentions to adapt the current text.

Acute toxicity, skin and eye irritation, and skin sensitisation

In the data matrix given in your category justification document [redacted] you have provided the summary of the data that is available for physico-chemical properties, ecotoxicity and for human health endpoints.

In order to support your claim that the substances included in the category have similar properties for the endpoints under consideration in the read-across approach, you refer to the acute toxicity, skin irritation, eye irritation, skin sensitisation properties of the category members.

You have pointed out that "*For the toxicological endpoints, in general there was low systemic toxicity in the whole subgroup (LD50 oral and dermal > 2000 mg/kg bw), except for one substance with mainly C12 carbon chain length composition (CAS No 90268-36-3) which showed an oral LD50 of 580 mg/kg bw. For the local skin and eye irritation, a general common behaviour was observed for the mono-ester subgroup: skin irritation (CLP category 2), and eye irritating (CLP category 1). Toxicological data further demonstrated that the substances of this subgroup were not sensitizing.* "

ECHA notes that some of the substances are not classified for skin irritation or eye damage based on experimental data, whereas some other substances are classified for these effects. ECHA therefore observes, that the category members have dissimilar toxic properties for these endpoints. The same applies to the acute toxicity, where the test results differ.

ECHA concludes that you have provided data, which suggests that the repeated dose toxicity of two category members differs. Furthermore, you have reported different acute toxicity values and different classification concerning skin and eye irritation among the category

members. This information contradicts with your proposed prediction, which is based on similar toxicological properties. Consequently, you have not demonstrated the validity of your hypothesis.

Data matrix, missing data

Annex XI, Section 1.5 of the REACH Regulation requires that "*Substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as a group, or "category" of substances*". A number of factors contribute to the robustness of a category. According to the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.6.2, Section R.6.2.1.5.f, (version 1.0, May 2008), one of these factors is the density and distribution of the available data across the category. In order to identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the category members needs to be available.

Consequently, the category justification should include a comparison of the existing experimental data for the category members, e.g. in a from of a data matrix. There should be sufficient existing data to support your hypothesis and the method of prediction.

You have referred to the available source information for the endpoints under consideration and concluded that the category members are "*not genotoxic (nor carcinogenic) and not toxic to reproductive and developmental toxicity*". ECHA observes that the **data density** across the category is limited based on the information provided in the read-across justification document and technical dossier of category members. Specifically, *in vitro* cytogenicity test (CA) and *in vitro* gene mutation test in mammalian cells data are available for **only one** category member [5]. Moreover, for one category member, i.e. substance [4] no toxicity study has been provided, and therefore any read-across *from* that substance or *for* that substance cannot be justified with similarity of toxicological effects.

ECHA considers that one data point or study cannot not cover the structural variation within the category domain. Furthermore, ECHA considers that with only one study, **similarity among** the category members cannot be established for the endpoints in question (i.e. genotoxicity). Consequently, the data do now allow overall conclusions on the endpoints under consideration. Therefore, predictions cannot be based on the matrix you have provided as it fails to demonstrate similarity among the category members.

In your comments to the draft decision, you indicated that you agree that the data is limited to CAS 90268-36-3; additional testing will be discussed under the Substance specific section. You provide a concise table which outlines the studies as requested by ECHA for all member of the Monoester group. You indicate that you agree that limited toxicological information is available, and that 'bridging studies' for the mutagenicity, developmental and reproductive toxicity properties will strengthen the read across approach. You indicate in Table 2, your testing plan, the studies that will be performed as 'bridging' studies in Phase 1. ECHA acknowledges your testing plan in Table 2. ECHA recognises that it partly follows the information requirement in the draft decisions on the member substances of the category. Concerning the Phase 3 of the plan, ECHA understands that the testing made at that phase depends on the results obtained in the phases 1 and 2. ECHA cannot pre-approve a testing plan that depends on study results, which will only be available in future. Therefore, ECHA will not amend or revise the information requirement made in the draft decision. In case the registrant will, in their dossier update, provide an adaptation of data that has been requested, based on phase 1 and 2 study results, it is the responsibility of the registrant to justify and document their adaptation according to the rules set out in REACH Annex XI or in column two

of the relevant Annexes (VIII-IX). ECHA will evaluate those adaptations in the follow-up phase of the compliance check.

You also request prolongation of the decision deadline in line with your testing plan. ECHA has assessed and responded to your request to prolong the decision deadline below.

ii. Conclusion on the read-across approach for toxicological properties

Because of the deficiencies explained above, ECHA considers that your read-across justification and documentation do not support your claim of 'similarity' among in the category members. Your read-across justification lacks evidence substantiated by adequate and reliable data that are required to support the read-across hypothesis. Therefore, your read-across hypothesis is not a reliable basis, whereby the properties of the members of the category may be predicted from data for source substance(s) within the group by interpolation to other substances in the group.

Thus, the adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. Therefore, ECHA rejects all adaptations in the technical dossier that are based on Annex XI, Section 1.5

I. IDENTITY OF THE SUBSTANCE

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

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

"Name or other identifier of the substance" is an information requirement as laid down in Annex VI, Section 2.1 of the REACH Regulation. The name and other identifiers are used to identify the substance in an unambiguous manner and are therefore fundamental for substance identification. Adequate information needs to be present in the technical dossier for the registered substance to meet this information requirement.

According to chapter 4.2.1 of the Guidance for identification and naming of substances under REACH and CLP (Version: 1.3, February 2014) – referred to as "the SID Guidance" thereinafter, a mono-constituent substance is a substance in which one constituent is present at a concentration of at least 80% (w/w) and which contains up to 20% (w/w) of impurities.

In contrary, according to chapter 4.3. of the SID Guidance, substances of Unknown or Variable composition, Complex reaction products or Biological material (UVCB substances), cannot be sufficiently identified by their chemical composition, because:

- The number of constituents is relatively large and/or
- The composition is, to a significant part, unknown and/or
- The variability of composition is relatively large or poorly predictable.

As a consequence, UVCB substances require other types of information for their identification, in addition to what is known about their chemical composition. For example, in addition to the chemical name, a detailed description of the manufacturing process should be provided.

You have identified your substance as a mono-constituent substance, using the following identifiers: EC No 253-452-8 (EC name disodium C-isodecyl sulphonatosuccinate) and CAS

No 37294-49-8 (CAS name Butanedioic acid, 2-sulfo-, 1(or 4)-isodecyl ester, sodium salt (1:2)).

In IUCLID section 1.4, in the file named [redacted] you stated that: "*This is the main component in [redacted] Surfactant. The main component cannot be isolated from the product. Therefore, it was synthesized. [....] The carbon 13 and proton NMR spectra of the test substance show that the main component is a disodium alkyl sulfosuccinate of mixed branched alkyl chain lengths (C9-C11). A minor component is observed, which is identified as the hydrolysis product sulfosuccinic acid sodium salt. Due to the complexity of the mixture the mole percentages of each component could not be measured by NMR.*"

The identifiers used for the substance are generic, and refer to a substance which contains a mixture of C10 branched esters, with a variation of the sulfonate moiety position. This is in line with the statement above and the analytical data attached in section 1.4, which confirm that the main constituent "Disodium isodecyl sulfosuccinate" is not a single constituent, but a mixture of branched derivatives, with variability on the position of the sulfonate moiety (2 or 3).

Consequently, the substance should not be considered as a a mono-constituent substance, but rather as a UVCB substance, due to the branching of the alkyl chain, and the variability of the position of the sulfonate moiety.

Therefore, you are requested to change the substance type from mono-constituent to UVCB. Furthermore, according to chapter 4.3 of the SID Guidance the naming of UVCB substances shall consist of two parts: (1) the chemical name and (2) a more detailed description of the manufacturing process.

Therefore, you are requested to provide a description of the manufacturing process that would include:

- identity (in particular the alkyl chain distribution) and ratio of the starting materials;
- a description of the relevant manufacturing steps in the order they occur (including information on the reaction steps/mechanisms);
- the relevant plant operating parameters applied to control the composition (e.g. temperatures/pressures; solvents; catalysis types...);
- extraction/isolation steps (if applicable);
- clean-up/purification steps (if applicable)

The description of the manufacturing process shall be included in the "Description" field in IUCLID section 1.2.

You shall ensure to select the correct "type of substance" (i.e. UVCB) corresponding to the substance subject to this registration from the dropdown list in IUCLID section 1.1.

In your comments to the draft decision, you agree to provide the requested information.

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

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

You have reported in section 1.2 the following impurities:

[redacted]

In IUCLID section 1.4, in the file named [redacted] an HPLC/CAD chromatogram is reported on page 3, with 2 main peaks, identified in table 4.1 as [redacted] corresponding to the anion of the main constituent and [redacted] In the note to table 4.1 you reported that "*Minor quantities of the [redacted] and and [redacted] were also detected*".

On page 4 of the same file, you also stated that "*Because the alkyl chain varies in length from C9-C11, unique peak assignments for the carbons in the alkyl groups are not possible*".

On page 5, you included a ^{13}C-NMR, where you assign the peaks relative to the [redacted] and to the [redacted] (hydrolysis product).

[redacted] and [redacted] were detected in the Mass Spectrum (see the comment under figure 4.2 [redacted] however appropriate analytical methods for the identification and quantification of these two impurities have not been provided. Therefore, it is not clear how these 2 impurities were identified and quantified individually. If the quantification was done based on the starting material, this is not verifiable, since this information was not provided in the dossier.

Therefore, the composition of the substance cannot be confirmed with the current analytical data.

You are requested to describe how the composition has been derived, providing the description of the analytical method(s), and the results that have been used to determine such composition.

For [redacted] and [redacted] it should be clarified how the different alkyl chains have been identified and quantified. If the identification and quantification was based on the composition of the starting material, a clear identification of the starting material needs to be provided as also requested under point 1.

The description of the analytical methods, the results and any calculation done for deriving the compositional information of the substance, shall be provided in IUCLID section 1.4. The description shall be sufficient for the methods to be reproduced.

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

In your comments to the draft decision, you agree to provide the requested information.

3. Composition of the substance (Annex VI, Section 2.3.)

Annex VI, section 2.3 of the REACH Regulation requires that each registration dossier contains sufficient information for establishing the composition of the registered substance and therefore its identity.

In that respect, according to chapter 4.3 of the Guidance, you should note that for UVCB substances presenting a large number of constituents, such as the registered substance, the following applies:

- All constituents present in the substance with a concentration of ≥ 10 % shall be identified and reported individually;
- All known constituents and constituents relevant for the classification and/or PBT assessment of the registered substance shall be identified and reported individually; and
- Unknown constituents shall be identified as far as possible by a generic description of their chemical nature; and
- For each constituent and group of constituents, the typical, minimum and maximum concentration levels shall be specified.

On page 2 of the file attached in section 1.4 named [redacted] you have identified [redacted] On page 5 of the same report you have identified the minor component [redacted] (quantification not provided). These two constituents, have not been reported in the composition in section 1.2.

In addition, the impurities named [redacted] and [redacted] have been identified with a name indicating that the sulfonate moiety is only in position 2, whereas the main constituent has been identified with a generic name, indicating that the sulfonate group can be either in position 2 or 3.

According to the SID guidance, all known constituents should be reported in the compositional information.

First, [redacted] identified in the HPLC/CAD analysis, and [redacted] identified in the NMR spectra (but not quantified), have not been reported in the composition. In addition, due to the missing explanation on the meaning of "hydrolysis product", it is not clear if [redacted] is actually part of the substance (i.e. the hydrolysis process is occurring at the level of the manufacturing process, which is not provided), or if it is formed when preparing the analytical sample.

Second, for what concerns the two impurities reported in IUCLID section 1.2, [redacted] and [redacted] the variability in the position of the sulfonate moiety observed for the main constituent is expected also for the impurities. A fix position of the sulfonate moiety is not supported by any analytical data.

Consequently, you are requested to revise the composition including all the identified constituents.

First, if [redacted] is part of the substance (i.e. the hydrolysis process is occurring at the level of manufacturing the substance), then it should be reported in IUCLID section 1.2 with the relative concentration values. The quantification of this constituent should be provided in section 1.4.

If, however, this constituent is an "artefact", in other words present only in the analytical sample, this should be clearly explained in the analytical report.

Second, the impurities [redacted] and [redacted] shall be identified with a generic entry, that reflects the variation of the position of the sulfonate moiety, in line with the name of the main constituent.

The correct compositional information of the substance shall be provided in IUCLID section 1.2. You shall ensure that the reported composition is consistent with the description of the process used for the manufacturing of the registered substance, including the identity of the starting materials used. You shall also ensure that the composition is verifiable and therefore supported by a description of the analytical methods for the identification and quantification of the constituents required to be reported, as required under Annex VI, Section 2.3.7.

As explained in the section 4.3.1. of the SID guidance, the terms "main constituents" and "impurities" should not be regarded as relevant for UVCB substances, and all the constituents should be reported in the "constituents" block in IUCLID section 1.2 with the typical, minimum and maximum concentration levels.

Note that the composition is affecting also the way the substance is identified (i.e. UVCB) and named. Therefore, the name of the substance should also be in line with the compositional information and needs to be representative of the registered substance.

In your comments to the draft decision, you agree to provide the requested information.

II. SPECIFIC CONSIDERATIONS ON THE INFORMATION REQUIREMENTS

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

4. *In vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study (Annex VIII, Section 8.4.2.)

An "*In vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study" is a standard information requirement as laid down in Annex VIII, Section 8.4.2. 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 XI, Section 1.5. of the REACH Regulation by providing a study record for an *in vitro* micronucleus test OECD 487, made in 2013, with analogue substance [5], Butanedioic acid, sulfo-, 1-C12-18-alkyl esters, disodium salts, (EC No 290-836-4, CAS No 90268-36-3), reliability 2, according to GLP, the test result is negative.

However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is 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.

ECHA considers that the *in vitro* mammalian chromosome aberration test (test method OECD TG 473) and the *in vitro* mammalian cell micronucleus test (OECD TG 487) are appropriate

to address the standard information requirement of Annex VIII, Section 8.4.2. of the REACH Regulation.

In your comments you have indicated your principal agreement to perform the requested test in Appendix 1 of the draft decision and your step-wise testing plan. ECHA acknowledges that but has not, at this stage, accepted the step-wise testing plan or the further adaptations that may follow from it, as explained in chapter "Data matrix" above. ECHA will evaluate any further information in the follow-up stage of the process.

Concerning your request to prolong the decision deadline, ECHA has assessed and responded to it below.

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: *In vitro* mammalian chromosome aberration test (test method: OECD TG 473) or *in vitro* mammalian cell micronucleus study (test method: OECD TG 487).

5. *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

An "*In vitro* gene mutation study in mammalian cells" is an information requirement as laid down in Annex VIII, Section 8.4.3. of the REACH Regulation, "if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2." is obtained.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for an *in vitro* mammalian cell gene mutation test waived, OECD 476 made in 2013, with analogue substance [5], Butanedioic acid, sulfo-, 1-C12-18-alkyl esters, disodium salts, (EC No 290-836-4, CAS No 90268-36-3), reliability 2, according to GLP, the test result is negative.

However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is 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.

ECHA considers that the *in vitro* mammalian cell gene mutation tests using the *Hprt* and *xprt* genes (OECD TG 476) and the *in vitro* mammalian cell gene mutation tests using the thymidine kinase gene (OECD TG 490) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.3.

In your comments you have indicated your principal agreement to perform the requested test in Appendix 1 of the draft decision and your step-wise testing plan. ECHA acknowledges that but has not, at this stage, accepted the step-wise testing plan or the further adaptations that may follow from it, as explained in chapter "Data matrix" above. ECHA will evaluate any further information in the follow-up stage of the process.

Concerning your request to prolong the decision deadline, ECHA has assessed and responded to it below.

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: *In vitro* mammalian cell gene mutation test (test method: OECD TG 476 *or* OECD TG 490) provided that the study requested under section 1. has a negative result.

Deadline to submit the requested information in this decision

The timeline indicated in the draft decision to provide the information requested is 12 months from the date of adoption of the decision for the information requested.

In your comments on the draft decision, you requested an extension of the timeline to 48 months for the category based on your testing plan. You justified your request stating that for practical and animal protection reasons, you would strongly advice to perform the tests in 3 phases (12-18 months for phase 1, 12 - 18 months for phase 2 and 12-18 months for phase 3), so that best use can be made from the already performed studies. Therefore, you noted that the total time of at least 48 months seems most realistic and necessary to conduct qualitative studies.

ECHA notes that the genotoxicty studies do not involve any of the core parameters and endpoints, which are included in OECD TG 408 and OECD TG 414, and therefore the phases 1 and 2 genotoxicity studies cannot inform of the need or of the design of the higher tier studies at phase 3. More notably, read-across is endpoint specific and therefore studies supporting the read-across need to inform of the relevant endpoints/effects.Therefore, ECHA did not extend the deadline in the draft decision.

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 25 July 2018.

ECHA notified you of the draft decision and invited you to provide comments within 30 days of the notification.

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 adopted the decision under Article 51(3) of REACH.

EUROPEAN CHEMICALS AGENCY

Appendix 3: Further information, observations and technical guidance

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

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements 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 tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.