~~Confidential~~

Helsinki, 09 March 2022

Addressees
Registrant(s) of 664-492-4_JS as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
11/05/2020

Registered substance subject to this decision ("the Substance")
Substance name: D-Glucopyranose, oligomeric, C10-16-alkyl glycosides, 2-hydroxy-3-sulfopropyl ethers, sodium salts
EC number: 664-492-4

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 ***16 March 2023***.

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. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. / OECD TG 471)

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

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

B. Information required from all the Registrants subject to Annex VIII of REACH

1. If negative results are obtained in test performed for the information requirement of Annex VII, Section 8.4.1. then: In vitro gene mutation study in mammalian cells

2. Short-term repeated dose toxicity (28 days; Annex VIII, Section 8.6.1.) to be combined with the Screening for reproductive/developmental toxicity below

3. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats

4. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD TG 203)

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

- Appendix entitled "Reasons common to several requests";

- Appendices entitled "Reasons to request information required under Annexes VII to VIII of REACH", respectively.

Information required depends on your tonnage band

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

- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

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 Mike Rasenberg, 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 read-across approach under Annex XI, Section 1.5.

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.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

ECHA has considered the scientific and regulatory validity of your grouping and read-across approach in general before assessing the specific standard information requirements in the following appendices.

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 (addressed under 'Scope of the grouping'). 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 R.6. and related documents[2,3].

A. Scope of the grouping

a. Description of the grouping

In your registration dossier you refer to a group (category) of 'alkyl polyglucosides (APGs)'. You have provided a read-across justification document in IUCLID Section 13, which refers to a publication (Cosmetic Ingredient Review (CIR) on APGs, 2013). However, you did not provide this publication in your dossier.

For the purpose of this decision, the following abbreviations are used for the group members:
[1] C10-16 alkyl glucoside / D-Glucopyranose, oligomeric, C10-16-alkyl glycosides (EC No. 600-975-8, CAS No.110615-47-9);
[2] Lauryl glucoside / dodecyl D-glucoside (EC No. 248-685-7 / CAS No. 27836-64-2).

You define the the structural basis for the grouping as "*the alkyl substituents range from 2 to 22 carbons in length, and the D-glycopyranosides consist of glucose-type mono-, di-, tri-, oligo-. or polysaccharides […]*". ECHA understands that this is the applicability domain of the grouping and will assess your predictions on this basis.

[2] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (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://doi.org/10.2823/794394

b. Assessment of the grouping

ECHA notes the following shortcomings with regards to your grouping approach.

1. 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 structural similarity may be considered as a group.*"

According to the Guidance on IRs and CSA, Section R.6, "*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 members (Guidance on IRs and CSA, Section R.6.2.4.1.). Therefore, qualitative and quantitative information on the compositions of the category members must 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 (Guidance on IRs and CSA, Section R.6.2.5.5.).

As indicated above, your definition of the applicability domain of the category can be summarised as: alkyl polyglucosides with an alkyl substituent range from 2 to 22 carbons in length, and D-glycopyranosides consisting of glucose-type mono-, di-, tri-, oligo-. or polysaccharides.

Your read-across justification document contains limited compositional information for the members of your category, in particular for the source substances.

No information on the degree -or absence- of D-glycopyranoside polymerisation and on alkyl chain length is provided for the constituents of the category members. Similarly, no analysis of the ratio of mono-, di-, tri-, oligo-. or polysaccharides is available from your dossier. Ranges of values related to polymerisation and alkyl chain length constitute criteria for inclusion in or exclusion from the category.

In the absence of qualitative and quantitative information on the compositions of the category members, the category membership of these substances cannot be confirmed.

2. Applicability domain of the category

A category (grouping) hypothesis should address "*the set of inclusion and/or exclusion rules that identify the ranges of values within which reliable estimations can be made for category members for the given endpoint"* (Guidance on IRs and CSA, Section R.6.2.4.1.). Particularly, "*the applicability domain of a (sub)category would identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made for the (sub)category members*" (Guidance on IRs and CSA, Section R.6.2.1.2.). Therefore, to reliably predict properties within a category the applicability domain should be described including the borders of the category, for which chemicals the category does not hold and a justification for the inclusion and/or exclusion rules.

As indicated above, your definition of the applicability domain of the category can be summarised as: alkyl polyglucosides with an alkyl substituent range from 2 to 22 carbons in length, and D-glycopyranosides consisting of glucose-type mono-, di-, tri-, oligo-. or polysaccharides.

This applicability domain does not introduce unambiguous inclusion/exclusion criteria which would identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made for the category members.

For instance, you indicate that "*The main difference between the substance D-Glucopyranose, oligomeric, C10-16-alkyl glycosides, 2-hydroxy-3-sulfopropyl ethers, sodium salts and the APG is the removal of the sulphonate grouping".* However, no inclusion and exclusion criteria for substitutions other than alkylation are defined in your read-across justification.

The Substance is not described in your justification as part of the category and category membership of the Substance cannot be confirmed. Therefore, you have not demonstrated that the read-across predictions cover the Substance.

B. Predictions for properties

a. Prediction for toxicological properties

You have provided the following reasoning for the prediction of toxicological properties: "*The main difference between the substance D-Glucopyranose, oligomeric, C10-16-alkyl glycosides, 2-hydroxy-3-sulfopropyl ethers, sodium salts and the APG is the removal of the sulphonate grouping. The* [redacted] *of the substance D-Glucopyranose, oligomeric, C10-16-alkyl glycosides, 2-hydroxy-3-sulfopropyl ethers, sodium salts. It is also found in small quantities in this UVBC. Removal of the sulphonate group is not believed to be toxicologically significant. Sulphonates are not normally considered a hazardous group of chemicals with many used in cosmetics and household products. […] it has been assessed that the information that has been published on APG's in the CIR review document "Safety Assessment of Decyl Glucoside and Other Alkyl Glucosides as Used in Cosmetics" is suitable for read-across in this registration".*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

You intend to predict the properties for the category members from information obtained from the following source substances:

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

- C10-16 alkyl glucoside; *in vitro* chromosomal aberration study according to OECD TG 473 (2013)

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

- C10-16 alkyl glucoside; subchronic repeated dose toxicity study according to OECD TG 408 (2013)

Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

- Lauryl glucoside; screening study for reproductive and developmental toxicity

according to OECD TG 421 (2013) and One-Generation Reproduction Toxicity Study according to OECD TG 415 (2013).

ECHA notes the following shortcomings with regards to predictions of toxicological properties.

1. *Composition of the substances within the group*

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 structural similarity may be considered as group.*"

According to the Guidance on IRs and CSA Section R.6, "*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 members (Guidance on IRs and CSA, Section R.6.2.4.1.). Therefore, qualitative and quantitative information on the compositions of the category members must be provided to allow assessing whether the attempted predictions are compromised by the composition and/or impurities.

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 (Guidance on IRs and CSA, Section R.6.2.5.5.).

The Substance is a UVCB substance. You do not sufficiently describe the composition of the category members (see above). Furthermore, for the source studies provided in the technical dossier that were conducted with these substances, as listed above, no information on the composition of the test material used to generate the source data is provided (see below under '*Adequacy and reliability of source studies*').

In addition, some quantitative information on the Substance for comparing with the source substances are not provided. In particular, the amount of one of the unreacted starting materials [redacted] is not quantified whereas it is listed as a constituent of the Substance in your dossier.

Without this information, no qualitative or quantitative comparative assessment of the compositions of the different category members can be completed. Therefore, it is not possible to assess whether the attempted predictions are compromised by the composition of the category members.

2. *Adequacy and reliability of source studies for repeated dose toxicity and reproductive toxicity*

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

- 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);
- cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

Specific reasons why the studies on the source substances do not meet these criteria are explained further below under the applicable information requirement sections B.2 and B.3. Therefore, no reliable predictions can be made for these information requirements.

3. Supporting information for repeated dose toxicity and reproductive toxicity

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" (Guidance on IRs and CSA, Section R.6.2.2.1.f.). 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 other category members.

Supporting information must include bridging studies to compare properties of the category members.

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

For the Substance, no study on repeated dose toxicity or reproductive toxicity is provided in the registration dossier. You only indicate in your read-across justification, without substantiation, that the main difference with APGs is the removal of the sulphonate group and that removal of the sulphonate group is not believed to be toxicologically significant.

For the source substances, you provide the studies used in the prediction of repeated dose toxicity and reproductive toxicity in the registration dossier. Apart from those studies, your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data for the source substances that would confirm that both the Substance and source substances cause the same type of effects.

Your dossier does not contain bridging studies with both the Substance and source substances that would allow comparison of their properties regarding repeated dose toxicity and reproductive toxicity.

Furthermore, specific reasons why the source studies cannot be considered reliable are explained further below under the relevant information requirement sections B.2 and B.3. Thus, the data set reported in the technical dossier does not include relevant, reliable and adequate information for the category members to support your read-across hypothesis.

In the absence of such information, you have not established that the category members are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

C. Conclusions on the grouping of substances and read-across approach

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

You have adapted the following standard information requirements by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2:

- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

Your weight of evidence adaptation raises the same decifiencies 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 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.

However, for each relevant information requirement, 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. Your weight of evidence approach 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.

These issues identified below are essential for all the information requirements in which you invoked a weight of evidence.

a. Reliability of the read across approach

Section 1 of the present Appendix identifies deficiencies of the grouping and read across approach used in your dossier. These finding apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptations.

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. In vitro gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

You have provided a key study in your dossier:

i. OECD TG 471 study (2009) with the Substance with the following strains, TA 98, TA 100, TA 1535, TA 1537, and E. coli WP2, which all gave negative results.

We have assessed this information and identified the following issue(s):

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[4] (1997). Two of the key parameters of this test guideline include:

a) The maximum dose tested must induce a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration must correspond to 5 mg/plate or 5 µl/plate.
b) The mean number of revertant colonies per plate must be reported for the treated doses and the controls.

The reported data for the study you have provided did not include:

a) a maximum concentration of 5 mg/plate or 5 µl/plate or that induced a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. You do not report any precipitation of the Substance and indicate that the maximum concentration tested was 5 µg/plate in the absence of any cytotoxicity.
b) data on the number of revertant colonies per plate for the treated plates and the controls. You did not provide any detail on the study results.

The information provided does not cover the above key parameters required by OECD TG 471.

Therefore, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable.

2. 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 provided the following information:

i. A key study (2017) according to OECD TG 202 with the Substance
ii. A key study (2002) according to ESA SOP 101 based on USEPA with the Substance

We have assessed this information and identified the following issues

a) Key study (i)

[4] ECHA Guidance R.7a, Table R.7.7–2, p.557

To fulfil the information requirement, a study must comply with OECD TG 202 (Article 13(3) of REACH). Therefore, the following specifications must be met:

- the percentage of immobilised daphnids is ≤ 10% at the end of the test in the controls (including the solvent control, if applicable);
- the number of immobilised daphnids is determined at 24 and 48 hours. Data are summarised in tabular form, showing for each treatment group and control, the number of daphnids used, and immobilisation at each observation;
- adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations are provided.

Your registration dossier provides an OECD TG 202 showing the following:

- the percentage of immobilised daphnids at the end of the test in the controls is not provided;
- tabulated data on the number of immobilised daphnids after 24 and 48 hours for each treatment group and control are not reported;
- the results of the analyses to determine the concentration of the test substance in the test vessels are not provided.

Based on the above, the validity criteria of OECD TG 202 are not met and the reporting of the study is not sufficient to conduct an independent assessment of its reliability. Therefore, the requirements of OECD TG 202 are not met.

b) Key study (ii)

Under Annex XI, Section 1.1.2., an existing study must:

- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 202.

Therefore, the following specifications must be met:

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;
- the concentrations of the test material are measured at least at the highest and lowest test concentration, at the beginning and end of the test.

Your registration dossier provides an ESA SOP 101 based on USEPA showing the following:

- no analytical monitoring of exposure was conducted;

Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability since the absence of analytical monitoring may result in an underestimation of the investigated effects. Therefore, the requirements of OECD TG 202 are not met.

On this basis, the information requirement is not fulfilled.

3. Growth inhibition study aquatic plants

Growth inhibition study aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

You have provided the following information:

i. A key study (2008) according to USEPAS OPPTS 840.5400 and USEPA Method 1003.0. with the Substance

We have assessed this information and identified the following issues:

Under Annex XI, Section 1.1.2., an existing study must:

- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 201.

Therefore, the following specifications must be met:

- 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. Growth must be expressed as the logarithmic increase in biomass (average specific growth rate) during the exposure period;
- 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%;
- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (*i.e.* detection and quantification) and working range must be available.
- the concentrations of the test material are measured at least at the beginning and end of the test:
    1) at the highest, and
    2) at the lowest test concentration, and
    3) at a concentration around the expected EC50.

Your registration dossier provides an USEPAS OPPTS 840.5400 and USEPA Method 1003.0.showing the following:

- EC50 and NOEC based on growth rate is not provided;
- section-by-section growth rates in the control cultures (0-24h), (24-48h) and (48-72h) are not reported;
- there is no information on biological results (cell count) for each replicate of control and test concentration at each time point (every day);
- no analytical monitoring of exposure was conducted.

Based on the above, the key parameter of OECD TG 201 is not covered and the reporting of the study is not sufficient to conduct an independent assessment of its reliability, including, for example, since the absence of analytical monitoring may result in an underestimation of the investigated effects. Therefore, the requirements of OECD TG 201 are not met.

On this basis, the information requirement is not fulfilled.

Appendix B: Reasons to request information required under Annex VIII of REACH

1. In vitro gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

a. Triggering of the study

Your dossier contains (i) a negative result for *in vitro* cytogenicity study in mammalian cells, and (ii) inadequate data for the other study (*in vitro* gene mutation study in bacteria).

The *in vitro* gene mutation study in bacteria provided in the dossier is rejected for the reasons provided in section A.1.

The result of the request for information in section A.1 will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

b. Assessment of information provided

You have provided the following studies in your dossier:

i. *in vitro* gene mutation study in bacteria according to OECD TG 471 (2009), with the Substance
ii. *in vitro* chromosomal aberration study in mammalian cells according to OECD TG 473 (2017), with the Substance
iii. *in vitro* chromosomal aberration study in mammalian cells according to OECD TG 473 (2013), with the analogue substance C10-16 alkyl glucoside (EC No. 600-975-8, CAS No. 110615-47-9).

You have also provided an adaptation, by indicating that: *"There is sufficient information regarding this end point from the three in-vitro test data already reported."* ECHA understands that you seek to adapt this information requirement according to the general rules for adaptation of Annex XI, Section 1.2. (weight of evidence).

We have assessed this information and identified the following issue(s):

As explained in the *Appendix on Reasons common to several requests* your weight-of-evidence adaptation is rejected.

Specific reasons why no reliable predictions can be made from studies (i), (ii) and (iii) are further explained below.

Based on the presented sources of information (i), (ii) and (ii), you argue that the available data give sufficient information to conclude that the Substance does not induce gene mutations in mammalian cells.

Relevant information that can be used to support weight-of-evidence adaptation for information requirement of Section 8.4.3 at Annex VIII includes similar information that is produced by the OECD TG 476/490 and OECD TG 488. This includes:

a) Detection and quantification of gene mutations (point mutations, frame-shift mutations, small deletions, etc.) including data on the frequency of mutant colonies in cultured mammalian cells (*in vitro*) or mutant frequency for each tissue in mammals (*in vivo*).

None of the sources of information (i), (ii) or (iii) provides relevant information on detection and quantification of gene mutation in cultured mammalian cells: source of information (i) investigates gene mutation in bacteria and sources of information (ii) and (iii) investigate chromosomal aberrations in mammalian cells but not gene mutation. In addition, as explained in the '*Appendix on Reasons common to several requests*', your read-across adaptation is rejected and source of information (iii) is considered unreliable.

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 properties foreseen to be investigated in an *in vitro* gene mutation study in mammalian cells. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

Consequently, you are required to provide information for this endpoint, if the *in vitro* gene mutation study in bacteria requested in section A.1 provides a negative result.

Study design

To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

2. Short-term repeated dose toxicity (28 days)

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII to REACH (Section 8.6.1.).

You have provided an adaptation according to Annex XI, Section 1.2 in your dossier.

In support of your adaptation you have provided the following study:

i. Sub-chronic repeated dose toxicity study (90 days) claimed to have been performed according to OECD TG 408 (2013), with the analogue substance C10-16 alkyl glucoside (EC No. 600-975-8, CAS No.110615-47-9).

We have assessed this information and identified the following issues:

As explained under *Appendix on Reasons common to several requests*, the weight of evidence adaptation 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.

a. Only one source of information

Annex XI, Section 1.2 states that there may be sufficient weight of evidence "*from several independent sources of information*".

You have only provided one source of information (study (i)).

b. Invalid read-across

As explained in the *Appendix on Reasons common to several requests* your read-across adaptation is rejected.

Specific reasons why no reliable predictions can be made from study (i) are further explained below.

1. *Incomplete robust study summary*

As explained in the *Appendix on Reasons common to several requests*, the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3). In order to make an independent assessment of a key study, a robust study summary must be provided (Guidance on IRs and CSA, Section R.6.2.6; Art. 3(28) and 10(a)(vii) and Annex I, Section 1.1.4/3.1.5 of REACH).

Robust study summary must provide a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study (Article 3(28)).

In your dossier, you have identified the source study (i) but provided only the no observed adverse effect level (NOAEL) value and a short extract from a publication summarising the main study results (CIR review, 2013). In addition, you acknowledge that the CIR review does not give full details on the exact test method used, the testing laboratory and the GLP status.

Therefore, you have not provided detailed information on the methods, results and conclusions, allowing for an independent assessment of the study. In the absence of such information, the study cannot be considered to provide an adequate and reliable coverage of the key parameters foreseen to be investigated in a study under to the corresponding OECD TG.

2. *Test material*

As explained in the *Appendix on Reasons common to several requests*, if the grouping concept is applied then in all cases the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment.

In order to predict the properties of the Substance, the test material used in the study on the source substance must be representative for the source substance (Article 10 and Recital 19 of REACH; Guidance on IRs and CSA, Section R.4.1.). 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.

You have identified the test material as C10-16 alkyl glucoside (CAS 110615-47-9), without further information, including composition of the test material.

In the absence of the information on the identity, composition, impurities of the test material, you have not demonstrated that the test material is representative for the source substance. Therefore, the study is not adequate for the purpose of classification and labelling and/or risk assessment.

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

Study design

When there is no information available neither for the 28-day repeated dose toxicity endpoint (EU B.7, OECD TG 407), nor for the screening study for reproductive/ developmental toxicity (OECD TG 421 or TG 422) (as explained below under section B.3), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG

407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1.[5]

Referring to the criteria in Annex VIII, Section 8.6.1, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the Substance is a liquid of low vapour pressure. Although the information provided in your dossier indicates that human exposure to the Substance by the inhalation route is possible, there is no evidence available showing that internal exposure through inhalation would be higher than though the oral route.

Therefore the Combined repeated dose toxicity study with the reproduction/developmental toxicity screening study must be performed according to the OECD TG 422, in rats and with oral administration of the Substance.

3. Screening for reproductive/developmental toxicity

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have provided an adaptation according to Annex XI, Section 1.2 in your dossier.

In support of your adaptation you have provided the following studies:

i. Screening for reproductive/developmental toxicity study claimed to have been performed according to OECD TG 421 (2013) with the analogue substance Lauryl glucoside (EC No. 248-685-7 / CAS No. 27836-64-2)
ii. One-generation reproduction toxicity study claimed to have been performed according to OECD TG 415 (2013) with the analogue substance Lauryl glucoside (EC No. 248-685-7 / CAS No. 27836-64-2)

We have assessed this information and identified the following issues:

As explained under *Appendix on Reasons common to several requests*, the weight of evidence adaptation 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.

Relevant information that can be used to support weight-of-evidence adaptation for information requirement of Section 8.7.3 at Annex VIII includes similar information that is produced by the OECD TG 421 or OECD TG 422. At general level, it includes information on the following key elements: 1) sexual function and fertility, 2) toxicity to offspring, and 3) systemic toxicity.

The sources of information (i) and (ii) provide relevant information on all aspects of sexual function and fertility, toxicity to offspring, and systemic toxicity. However, these sources of information have deficiencies affecting their reliability as further explained below.

a. Invalid read-across

As explained in the *Appendix on Reasons common to several requests* your read-across

[5] ECHA Guidance, Section R.7.6.2.3.2., pages 484 to 485 of version 6.0 – July 2017. (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf)

adaptation is rejected.

Specific reasons why no reliable predictions can be made from study (i) or (ii) are further explained below.

1. *Incomplete robust study summaries*

As explained in the *Appendix on Reasons common to several requests*, the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3). In order to make an independent assessment of a key study, a robust study summary must be provided (Guidance on IRs and CSA, Section R.6.2.6; Art. 3(28) and 10(a)(vii) and Annex I, Section 1.1.4/3.1.5 of REACH).

Robust study summary must provide a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study (Article 3(28)).

In your dossier, you have identified the source studies (i) and (ii) but provided only the no observed adverse effect level (NOAEL) values and short extracts from a publication summarising the main study results (CIR review, 2013). In addition, full details on the exact test method used, the testing laboratory and the GLP status are not provided.

Therefore, you have not provided detailed information on the methods, results and conclusions, allowing for an independent assessment of the studies. In the absence of such information, the studies cannot be considered to provide an adequate and reliable coverage of the key parameters foreseen to be investigated in a study under to the corresponding OECD TG.

2. *Test material*

As explained in the *Appendix on Reasons common to several requests*, if the grouping concept is applied then in all cases the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment.

In order to predict the properties of the Substance, the test material used in the study on the source substance must be representative for the source substance (Article 10 and Recital 19 of REACH; Guidance on IRs and CSA, Section R.4.1.). 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.

You have identified the test materials as Lauryl glucoside (CAS No. 27836-64-2) *"as APG C12-C14 fatty alcohol from renewable sources, n: 1.43"* in study (i) and as Lauryl glucoside (CAS No. 27836-64-2) *"as C10-14 or C10-16, n: 1.4)"* in study (ii), without further information, including composition of the test material.

In the absence of the information on the identity, composition, impurities of the test materials, you have not demonstrated that the test material is representative for the source substance. Therefore, the study is not adequate for the purpose of classification and labelling and/or risk assessment.

Therefore, the sources of information provide relevant information on all aspects of sexual function and fertility, toxicity to offspring, and systemic toxicity. However, the reliability of these sources of information is significantly affected.

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 properties foreseen to be investigated in an OECD TG 421 or OECD TG 422 study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

Study design

When there is no information available neither for the 28-day repeated dose toxicity endpoint (EU B.7, OECD TG 407) (as explained above under section B.2), nor for the screening study for reproductive/ developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1.[6]

Therefore, a study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral[7] administration of the Substance.

4. Short-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

You have provided the following information:

i. A key study (2008) according to ESA SOP 117 based on USEPA (2002).

We have assessed this information and identified the following issues:

Under Annex XI, Section 1.1.2., an existing study must:

- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 203.

Therefore, the following specifications must be met:

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available.
- the determinations of exposure concentrations reflect the concentrations of the dissolved chemical;

Your registration dossier provides an ESA SOP 117 based on USEPA (2002) showing the following:

- no analytical measurement of test concentrations was conducted.

Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability since the absence of analytical monitoring may result in an underestimation of the investigated effects. Therefore, the requirements of OECD TG 202 are not met.

On this basis, the information requirement is not fulfilled.

[6] ECHA Guidance R.7a, Section R.7.6.2.3.2., pages 484 to 485 of version 6.0 – July 2017. (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf)
[7] ECHA Guidance R.7a, Section R.7.6.2.3.2.

Appendix C: 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:

a) the boundary composition(s) of the Substance,
b) the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

2. Information on the Test Material needed in the updated dossier

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

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance.

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 D: 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 E: 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 17 November 2020.

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

ECHA did not receive any comments within the commenting period.

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 F: 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)[12]

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[13]

[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] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[13] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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

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

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

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

Appendix G: 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.