Helsinki, 10 December 2019

Addressee: [redacted]

Decision number: CCH-D-2114493173-47-01/F
Substance name: Sodium p-cumenesulphonate
EC number: 239-854-6
CAS number: 15763-76-5
Registration number: [redacted]
Submission number: [redacted]
Submission date: 28/03/2018
Registered tonnage band: Over 1000

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. **In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, EU B.13/14. / OECD TG 471) with the registered substance;**

2. **In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490) with the registered substance, provided that the study requested under 1. have negative results;**

3. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) in a first species (rat or rabbit), oral route with the registered substance;**

4. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) in a second species (rat or rabbit]), oral route with the registered substance;**

5. **Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: Daphnia sp. Acute immobilisation test, EU C.2./OECD TG 202) with the registered substance;**

6. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: Alga, growth inhibition test, EU C.3./OECD TG 201) with the registered substance;**

7. **Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: Fish, acute toxicity test, OECD TG 203) with the registered substance;**

8. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with the registered substance;**

9. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with the registered substance;**

10. **Robust study summary (RSS) for [redacted], ready biodegradability (Annex VII, Section 9.2.1.1.);**

    OR

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: DOC die-away test, OECD TG 301A) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: CO2 evolution test, OECD TG 301B) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: MITI test (I), OECD TG 301C) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Closed bottle test, OECD TG 301D) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Modified OECD screening test, OECD TG 301E) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Manometric respirometry test, OECD TG 301F) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Ready biodegradability – CO2 in sealed vessels (headspace test), OECD TG 310)

    with the registered substance.

You have to submit the requested information in an updated registration dossier by ***15 September 2022***. You shall also update the chemical safety report, where relevant. The deadline has been set to allow for sequential testing.

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.

Authorised[1] by Ofelia Bercaru, Head of Unit, 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

I. Grouping and read-across approach for (eco)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 'hydrotropes' to predict from data for reference substance(s) missing (eco)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 gene mutation study in bacteria (Annex VII, Section 8.4.1.);
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.2.);
- Pre-natal developmental toxicity study (Annex IX, Section 8,7.2);
- Short-term toxicity testing on invertebrates (Annex VII, Section 9.1.1);
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2);
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3);
- Long-term toxicity testing on invertebrates (Annex IX, Section 9.1.5);
- Ready biodegradability (Annex VII, Section 9.2.1.1).

ECHA has considered the scientific and regulatory validity of your grouping and read-across approach in general before assessing the individual properties of the substance in Section II of 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 group or category.

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

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a toxicological or ecotoxicological 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/ ecotoxicological 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 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 foresees that there are two options which may form the basis of the read-across hypothesis[2, 3] - (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 (eco)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.

A. Scope of the category

You have provided a read-across justification document in IUCLID Section 13.

You have defined the structural basis for the category/grouping as simple salts (ammonium, calcium, potassium and sodium salts) of toluene, xylene and cumene sulphonic acids.

You have identified the following substances as 'Hydrotrope' category members:

[1] Sodium toluene-4-sulphonate (EC No. 211-522-5);
[2] Sodium (xylenes and 4-ethylbenzene) sulphonate (EC No. 215-090-9[4]);
[3] Calcium (xylenes and 4-ethylbenzene) sulphonate (EC No. 248-829-9);
[4] Ammonium (xylenes and 4-ethylbenzene) sulphonate (EC No. 943-024-5);
[5] Sodium cumene sulphonate (EC No. 239-854-6);
[6] Potassium cumene sulphonate (EC No. 629-764-9); and
[7] Ammonium cumene sulphonate (EC No. 253-519-1).

i. 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 their constituents to establish the extent of qualitative and quantitative differences and similarities in the structure and in the composition of these substances. ECHA recommends to follow its Guidance for identification

[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://echa.europa.eu/publications/technical-scientific-reports

[4] The current EC number for this substance is 701-037-1.

and naming of substances under REACH and CLP for all source substances within the category.

In Section 2.2. of the read-across justification document, you address the composition of the category members. The toluene and cumene sulphonates are mono-constituent substances whereas the (xylenes and 4-ethylbenzene) sulphonates are UVCB substances. Toluene-, cumene- and 4-ethyl- benzene sulphonate are mainly in the from of the para-isomer (approximately [redacted]). For xylene-benzene sulphonate the alkyl groups are mainly in the [redacted]).

ECHA considers the information with regard to the composition of the category members as sufficient in order to establish structural similarity (and structural differences) between the category members.

ii. Applicability domain of the category

According to the ECHA Guidance on information requirements and chemical safety assessment Chapter R.6.2, Section R.6.2.4.1, (version 1.0, May 2008) a category 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. These rules, can be described as the applicability domain for an endpoint and provide a means of extending the category membership to chemicals not explicitly included in the current definition of a category.*"

Furthermore, according to the ECHA Guidance on information requirements and chemical safety assessment Chapter R.6.2, Section R.6.2.1.2, (version 1.0, May 2008) "*a category evaluation does not necessarily result in all the individual substances included in the category evaluation being registered to the Agency, although the data from these substances will be included in the category report in support of the registration.*"

Based on your description of the structural basis of your grouping/category approach, ECHA understands that all category members share a common 'core structure' and that they vary only in terms of their alkyl- substitutions on the benzene ring. Furthermore, ECHA understands that the allowed substituents to the 'core structure' define the inclusion criteria for the category membership. You have described the applicability domain of the category as ammonium, calcium, potassium and sodium salts of cumene, toluene, and xylene sulphonic acids.

Considering the UVCB nature of the (xylene and 4-ethylbenzene) sulphonate, ECHA considers that the the applicability domain of the category is: ammonium, calcium, potassium and sodium salts of cumene, toluene, and xylene (containing [redacted] The structural variation within the category is defined by the type of cation and the sulphonic acid that forms the anion. Because ECHA accepts unrestricted read-across between the ammonium, calcium, potassium and sodium salts of each individual sulphonic acid provided that the source study is adequate and reliable for the endpoint concerned, the structural variation within this group is defined by the sulphonic acid used; i.e. cumene-, toluene-, and xylene (containing [redacted]. ECHA assessed your proposed predictions on this basis.

B. Prediction of toxicological properties

You have provided the following reasoning for the prediction of toxicological properties: *"The Hydrotrope category comprises seven substances which have similar chemical structures and demonstrate the same type of effects. [...] The same absence of or type of effect are observed for the different source substances. There are no relevant variations in the strength of the effects observed among the source substances and the same strength is predicted for the target substances".*

ECHA understands that you base your predictions on the assumption that different compounds have similar toxicological properties as a result of structural similarity. You assume that all substances will show the same absence of or type of effects for toxicological properties. ECHA notes the following shortcomings with regards to prediction of toxicological properties:

i. *Insufficient information to support a claim of the* same absence of or type of effects *toxicological properties*

According to Annex XI, Section 1.5., *'Application of the group concept requires that [...] human health effects [...] may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach).'*

A number of factors contributes to the robustness of the predictions made within a group. According to the ECHA Guidance on information requirements and chemical safety assessment Chapter R.6.2, Section R.6.2.1.5. (version 1.0, May 2008), one of these factors is the density and distribution of the available data across the category. In order 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.

In the read-across hypothesis, you assume that the same absence of or type of effects across the category. You argue that this is supported by the available studies on the various category members which demonstrate similar toxicity.
You have provided:

- Repeated dose toxicity studies with (xylenes and 4-ethylbenzene) sulphonate, toluene sulphonate and sodium cumenesulphonate;
- Pre-natal developmental toxicity studies in rats and rabbits conducted with (xylenes and 4-ethylbenzene) sulphonates;
- Reproductive and developmenal toxicity screening test conducted with a toluene sulphonate on toluene sulphonate;
- *In vitro* mutagenicity studies conducted with Sodium (xylenes and 4-ethylbenzene) sulphonate;
- *In vivo* micronucleus test and a sub-chronic toxicity study with Calcium (xylenes and 4-ethylbenzene) sulphonate and Sodium cumene sulphonate; and supporting toxicokinetic information available on toluene sulphonate.

ECHA notes that you predict (or propose to predict) the toxicological properties of the cumene- and toluene- sulphonates from the available data (or data to be generated on) (xylenes and 4-ethylbenzene) sulphonates thus the information available does not cover the range of structural variations. However, there is very little data available on the target

substances to support such a prediction for the human health endpoints of mutagenicity, developmental toxicity and toxicity to reproduction.

With regard to reading across from a (xylenes and 4-ethylbenzene) sulphonate to the toluene sulphonates (and *vice versa*), ECHA notes that the results from the available reproductive and developmental toxicity screening test conducted with a toluene sulphonate is consistent with the available repeated dose toxicity and pre-natal developmental toxicity studies conducted with the (xylenes and 4-ethylbenzene) sulphonates. In both cases, a lack of toxicity have been demonstrated up to the limit dose.

In addition, there is supporting toxicokinetic information available on toluene sulphonate which demonstrates that this substance is excreted unchanged in urine.

Therefore, ECHA considers it likely that the repeated dose, developmental toxicity and the toxicity to reproduction effects of toluene sulphonates may be predicted from (xylenes and 4-ethylbenzene) sulphonates or *vice versa*. However, for mutagenicity there is no data available for toluene sulphonate which allows for a side-by-side comparison of the effects. ECHA considers that, in the absence of any relevant mutagenicity data on toluene sulphonate, the available information does not support your claim of a regular pattern of same absence of and type of effects with regard to mutagenicity.

First, with regard to reading across from a (xylenes and 4-ethylbenzene) sulphonate to the cumene sulphonates (and *vice versa*) for human health endpoints other than mutagenicity, ECHA notes that the results of the sub-chronic toxicity study on cumene sulphonate is consistent with available information on (xylenes and 4-ethylbenzene) sulphonate and allow a side-by-side comparison of effects related to systemic toxicity which supports the read-across approach. However, a sub-chronic toxicity study does not allow assessment of potential effects related to developmental toxicity and toxicity to reproduction.
There are no toxicokinetic information available on either (xylenes and 4-ethylbenzene) sulphonate or the cumene sulphonates that could have helped supporting the read-across approach.

Therefore, in the absence of any relevant reproductive or developmental data on cumene sulphonate, ECHA considers that there is no support for the read-across for these endpoints. A reproductive and developmenal toxicity screening test (OECD TG 421/422) allows a screening level assessmet of such effects and could potentially be used to support read-across also for developmental toxicity and toxicity to reproduction provided that the results obtained are consistent with those obtained with the source substance.

Second, with regard to mutagenicity, ECHA notes that there is an *In vivo* micronucleus test available with a cumene sulphonate. The results of this study show no chromosome aberrations and are consistent with those obtained with (xylenes and 4-ethylbenzene) sulphonate. However, the *in vitro* tests for mutagenicity cover two aspect chromosome aberration and gene mutation. There is no information available which would allow comparison between the gene mutation potential of a cumene sulphonate and that of (xylenes and 4-ethylbenzene) sulphonate. In the absence of such data, ECHA considers that there is no support for your claim of a regular pattern of the same absence of and type of effects with regard to potential to induce gene mutation.

C. Prediction of ecotoxicological and ready biodegradability properties

You have provided the following reasoning for the prediction of ecotoxicological and ready biodegradability properties: *"The Hydrotrope category comprises seven substances which have similar chemical structures and demonstrate the same type of effects. [...] The same absence of or type of effect are observed for the different source substances. There are no relevant variations in the strength of the effects observed among the source substances and the same strength is predicted for the target substances".*

Specifically for ready biodegradability, you claim that *"The experimental data [..] is consistent and confirms the ready biodegradability of these substances. The data support the similar behaviour in the environment of this substances.".*

ECHA understands that you base your predictions on the assumption that different compounds have similar ecotoxicological and ready biodegradability properties as a result of structural similarity. ECHA notes the following shortcomings:

i. Inadequate source studies for aquatic toxicity endpoints

As required in Annex XI, Section 1.5. of the REACH Regulation, source studies should be adequate for the purpose of classification and labelling and/or risk assessment, have adequate and reliable coverage of the key parameters and cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3), and adequate and reliable documentation of the applied method shall be provided.

You have referred to the outcome of aquatic toxicity studies conducted with the category members to show similar ecotoxicological properties. ECHA has evaluated the source studies provided in the technical dossier of the category members and also referred to in your read-across document. Following this assessment, ECHA has identified several deficiencies.

First, in the following two short-term toxicity studies on *Daphnia magna* (limit studies), the concentration tested (i.e. 40.3 mg a.i./L) is below the threshold of 100 mg/L given in paragraph 24 of OECD TG 202:

1) Study with sodium cumene sulphonate [redacted] according to OECD TG 202, reliability 2.
2) Study with sodium xylene sulphonate [redacted] according to OECD TG 202, reliability 2.

In view of this deviation from OECD TG 202, ECHA concludes that these two studies are not adequate to conclude on the endpoint of short-term toxicity testing on invertebrates.

Second, the long-term toxicity test on *Daphnia magna* with sodium cumene sulphonate (*"Long-term toxicity to aquatic invertebrates.002"*, according to TG UBA Verlaengerter Toxizitaetstest bei Daphnia magna nach UBA (1984 standard)) has a reliability of 4 (Klimisch score). ECHA agrees that this study is not reliable, since it does not give sufficient experimental details and is only listed in short abstracts or secondary literature, as given in ECHA Guidance *Chapter R.4: Evaluation of available information* (version 1.1, December 2011).

Therefore, ECHA considers that these studies with the above mentioned deficiencies do not constitute adequate and reliable supporting information and cannot be used as source

studies.

ii. Insufficient information to support a claim of the same ecotoxicological and ready biodegradability properties

According to Annex XI, Section 1.5., '*Application of the group concept requires that [...] environmental effects or environmental fate may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach).*'

A number of factors contributes to the robustness of the predictions made within a group. According to the ECHA Guidance on information requirements and chemical safety assessment Chapter R.6.2, Section R.6.2.1.5. (version 1.0, May 2008), one of these factors is the density and distribution of the available data across the category. In order 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.

Ecotoxicological properties

In the read-across hypothesis, you assume the same ecotoxicological properties across the category. You further argue that this is supported by the available studies on the various category members which demonstrate similar "*low toxicity to aquatic organisms*" across the endpoints.

ECHA notes that you predict (or propose to predict) the ecotoxicological properties of the cumene sulphonates from the available data on (xylenes and 4-ethylbenzene) sulphonates and toluene sulphonate. However, there is no reliable data available on cumene sulphonates to support such a prediction for the endpoints of algae growth inhibition, short-term *Daphnia*, short-term fish.

ECHA notes the only studies available on cumene sulphonates are one short-term *Daphnia* test and one long-term *Daphnia* test. However, as explained above under point i "*Inadequate source studies for aquatic toxicity endpoints*", these studies are not adequate; hence, there is no reliable data available for cumene sulphonates and thus the available information does not cover the range of structural variations. Therefore, ECHA considers that the read-across is not supported.

Ready biodegradability property

In the read-across hypothesis, you assume the same ready biodegradability properties across the category. You further argue that this is supported by the available studies on the various category members which demonstrate the ready biodegradability of the substances and refer to the OECD HPV programme.

ECHA notes that you predict (or propose to predict) the ready biodegradability properties of the cumene sulphonates and of (xylenes and 4-ethylbenzene) sulphonates from the available data on toluene sulphonate (and *vice versa*).

ECHA notes that the source study on toluene sulphonate is valid. However, for the reasons explained in section 10 below, the studies available on cumene- and on (xylenes and 4-

ethylbenzene) sulphonates are either not adequate (four studies according to OECD TG 301B) or the information provided is insufficient to make an independent assessment of the study (two studies according to OECD TG 301D). As a consequence, there is currently no reliable information for cumene- and (xylenes and 4-ethylbenzene) sulphonates and thus the available information does not cover the range of structural variations. Therefore, ECHA considers that the read-across is not supported.

Further, ECHA points out that the OECD HPV programme report was not provided and could not be assessed. Moreover, this previous evaluation under the OECD HPV programme has not applied the requirements of Annex XI, Section 1.5 for predicting the properties of the category members. For these reasons, the reference to the previous evaluation under the OECD HPV programme does not provide a basis for adaptation under Annex XI, Section 1.5.

In conclusion, in the absence of any relevant aquatic toxicity data on cumene sulphonate and in the absence of reliable ready biodegradability data on cumene and (xylenes and 4-ethylbenzene) sulphonates, ECHA considers that there is no support for your claim of a regular pattern with the same ecotoxicological and ready biodegradability properties.

For your consideration, ECHA notes there may be information available on these substances that has not been included in the technical dossier nor in the data matrix for ecotoxicity even though such data may be relevant. For instance, in your read-across justification you propose read-across between the ammonium, calcium, potassium and sodium salts and each individual sulphonic acid. However, ECHA notes that there are aquatic toxicity studies available in the sulphonic acids technical dossiers that have not been considered and reported in the technical dossier of the corresponding salts (e.g. short-term fish and short-term *Daphnia* studies on toluene sulphonic acid). Furthermore, in your read-across justification you refer to the "Hydrotropes"category defined under OECD HPV programme. However, ECHA notes that for aquatic toxicity endpoints, not all studies cited in the OECD HPV Program report have been considered and reported in the technical dossier (e.g. short-term fish and short-term *Daphnia* studies on cumene sulphonate). Since these additional studies available in the technical dossiers of the sulphonic acids and in the OECD HPV Program report have not been included in the technical dossiers of the registered substance, they could not be taken into account when assessing the scientific and regulatory validity of your grouping and read-across approach of the hydrotropes category.

iii. *Inconsistency between the read-across hypothesis and the experimental results for short-term aquatic toxicity and ready biodegradability endpoints*

Annex XI, Section 1.5 of the REACH Regulation requires that "*Substances whose [..] 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 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*". The observation of a deviation in a trend among some members of a category is a warning sign. An explanation for this deviation in the trend resulting in a contradiction between the similarities in properties claimed in the read-across hypothesis and the observation of different properties needs to be provided and supported by scientific evidence.

Ecotoxicological properties

In the read-across hypothesis, you assume the same ecotoxicological properties across the category. You further argue that this is supported by the available studies on the various category members which demonstrate similar "*low toxicity to aquatic organisms*" across the endpoints.

In the available short-term *Daphnia* tests, toluene sulphonate is acutely more toxic than (xylenes and 4-ethylbenzene) sulphonates, *i.e.* 48h EC_{50} of 54 mg/L toluene sulphonate *versus* 48h EC_{50} values *>100* mg/L for (xylenes and 4-ethylbenzene) sulphonates. You have considered the study on toluene sulphonate as an "*outlier*" and used it only as supporting study. You provide no scientifically valid justification for ignoring this study, however ECHA considers this study as valid. The study provides evidence that the short-term toxicity to aquatic invertebrates differs between toluene- and (xylenes and 4-ethylbenzene)-sulphonates. Consequently, there is a contradiction between your read-across hypothesis of the same ecotoxicological properties among the category members and the available experimental data, and deviations are not explained. Therefore, ECHA considers that your read-across is not supported.

Ready biodegradability property

In the read-across hypothesis, you assume the same ready biodegradability properties across the category. You further argue that this is supported by the available studies on the various category members which demonstrate the ready biodegradability of the substances.

ECHA notes that the source study on toluene sulphonate is valid and shows that this substance is ready biodegradable. You use this study as a key study in order to conclude on this endpoint for all category members. Regarding the source studies available on cumene- and on (xylenes and 4-ethylbenzene) sulphonates, you report the following in Section 2.4.2 of the read-across justification: "*Consistent and similar biodegradation was seen in C2 evolutionary studies (OECD TG 301B) (..). Lower biodegradation rates were observed when using the oxygen consuption test (OECD 301D), although it was still concluded that the test substances (..)cumene sulphonate and (..)(xylenes and 4-ethylbenzene) sulphonate, were biodegradable.*" As explained in section 10 below, the OECD TG 301B studies, showing that these substances are readily biodegradable, are not adequate. Nevertheless, although ECHA cannot currently establish the reliability of the two OECD 301D studies, you consider them reliable since you have assigned Klimisch score 2. The results of these two OECD 301D studies, used as supporting studies, indicate that cumene and (xylenes and 4-ethylbenzene) sulphonate are not ready biodegradable and hence contradict your hypothesis that the category members are ready biodegradable. Therefore, ECHA considers that you have not demonstrated that the read-across is supported.

In conclusion, ECHA considers that the data available in your dossier do not support your claim of a regular pattern with the same ecotoxicological and ready biodegradability properties.

D. Registrants comments on the draft decision

i. Read-across for toxicological endpoints

In your comments to the draft decision, you propose to conduct a reproductive and developmental toxicity screening test (OECD TG 421) with Sodium cumene sulphonate (EC No. 239-854-6) prior to conducting the requested Pre-natal developmental toxicity studies. Should this "bridging infromation" confirm the assumed toxicity profile of the substance you propose to adapt the requests for Pre-natal developmental toxicity studies. If not you agree to conduct the Pre-natal developmental toxicity studies on Sodium cumene sulphonate (EC No. 239-854-6). ECHA cannot currently assess if your proposed testing strategy would be acceptable. ECHA will evaluate your information after the deadline of this decision according to the specific rules of column 2 adaptations and adaptation(s) according to Annex XI.

ii. Read-across for ecotoxicological endpoints

In your comments on the draft decision you indicate your intention to re-evaluate the category approach for the aquatic toxicity endpoints. You propose to complete first the requirements on short-term aquatic studies for Sodium cumene sulphonate (EC No. 239-854-6) (requests 5-7), as well as for the other category members. You will successively update the read-across justification based on the new and existing short-term aquatic toxicity data with the category members (or their corresponding acids). If also long-term aquatic studies need to be conducted (requests 8-9), you propose to choose the "*representative substance(s)*" to be tested based on the updated read-across justification. ECHA has addressed under requests 8-9 below your comments related to the necessity to conduct the long-term toxicity testing on aquatic invertebrates and on fish using an Integrated Testing Strategy (ITS).

ECHA acknowledges your intention to revise the read-across approach for aquatic toxicity endpoints after completing the requirements on short-term aquatic endpoints for the category members. However, since this information and an updated read-across justification for the long-term aquatic toxicity endpoints is not yet available, ECHA cannot currently assess whether your proposal to test "*representative substance(s)*" and use read-across adaptations for the long-term aquatic toxicity endpoints would be acceptable. ECHA will evaluate your information after the deadline of this decision according to the specific rules of column 2 adaptations and adaptation(s) according to Annex XI.

E. Conclusions

ECHA accepts unrestricted read-across between the ammonium, calcium, potassium and sodium salts of each individual sulphonic acid, i.e. cumene-, toluene- and (xylene and 4-ethyl benzene)- sulphonic acid; provided that the source study is adequate and reliable for the endpoint concerned.

i. Read-across for toxicological endpoints

Reading across from (xylene and 4-ethyl benzene) sulphonates to toluene sulphonate (and *vice versa*), for repeated dose toxicity, developmental toxicity and toxicity to reproduction "bridging information" is available and as a result ECHA accept the proposed read-across. However, ECHA considers that due to missing "bridging information" it is not possible to establish a scientifically credible link between the target and source substances which would allow to predict the outcome of the *in vitro* mutagenicity tests. Consequently, read-across is rejected for mutagenicity.

Reading across from (xylene and 4-ethyl benzene) sulphonates to cumene sulphonates (and *vice versa*), for repeated dose toxicity "bridging information" is available and as a result ECHA accept the proposed read-across. However, ECHA considers that due to missing "bridging information" it is not possible to establish a scientifically credible link between the target and source substances which would allow to predict the outcome of the *in vitro* mutagenicity tests, developmental toxicity studies, and toxicity to reproduction studies. Consequently, read-across is rejected for these endpoints.

ii. Read-across for ecotoxicological and ready biodegradability endpoints

Reading across from (xylene and 4-ethyl benzene) sulphonates to toluene sulphonate, ECHA considers that, due to the available data contradicting your read-across hypothesis, your proposed prediction for aquatic toxicity is not supported. Consequently, the proposed read-across is rejected.

Reading across from (xylene and 4-ethyl benzene) sulphonates and from toluene sulphonate to cumene sulphonates, ECHA considers that due to missing "bridging information" it is not possible to establish a scientifically credible link between the target and source substances which would allow to predict the outcome of the aquatic toxicity studies. Consequently, the proposed read-across is rejected.

Reading across from toluene sulphonate to (xylene and 4-ethyl benzene) sulphonates and to cumene sulphonates, ECHA considers that, due to insufficient reliable information and contradicting information, your proposed prediction for ready biodegradability is not supported. Consequently, the proposed read-across is rejected.

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 more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)

An "*In vitro* gene mutation study in bacteria" is a standard information requirement as laid down in Annex VII, Section 8.4.1. 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. However, as explained above in the section 'Grouping and read-across approach', your adaptation of the information requirement is rejected. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA considers that the bacterial reverse mutation test (test method EU B.13/14. / OECD TG 471) is appropriate to address the standard information requirement of Annex VII, Section 8.4.1. of the REACH Regulation.

In your comments on the draft decision, you agree to conduct the requested study. You also indicate that Sodium cumene sulphonate (EC No. 239-854-6) is the most appropriate substance to test since the sodium ion is ubiquitous in mammalian systems. ECHA agrees with this proposal and has amended the request to state the registered substance, only.

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: Bacterial reverse mutation test (test method: EU B.13/14. / OECD TG 471).

2. 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. However, as explained above in the section 'Grouping and read-across approach', your adaptation of the information requirement is rejected. 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 on the draft decision, you agree to conduct the requested study. You also indicate that Sodium cumene sulphonate (EC No. 239-854-6) is the most appropriate substance to test since the sodium ion is ubiquitous in mammalian systems. ECHA agrees with this proposal and has amended the request to state the registered substance, only..

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

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

A "pre-natal developmental toxicity study" (test method OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation. However, as explained above in the section 'Grouping and read-across approach', your adaptation of the information requirement is rejected. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid, ECHA concludes that testing should be performed by the oral route.

In your comments on the draft decision, you propose to conduct a reproductive and developmental toxicity screening test (OECD TG 421) with Sodium cumene sulphonate (EC No. 239-854-6) prior to conducting the requested Pre-natal developmental toxicity studies. Should this "bridging infromation" confirm the assumed toxicity profile of the substance you propose to adapt the requests for an OECD TG 414 studies. If not you agree to conduct the OECD TG 414 studies. ECHA cannot currently assess if your proposed testing strategy would be acceptable. ECHA will evaluate your information after the deadline of this decision according to the specific rules of column 2 adaptations and adaptation(s) according to Annex XI.
You also indicate that Sodium cumene sulphonate (EC No. 239-854-6) is the most appropriate substance to test since the sodium ion is ubiquitous in mammalian systems. ECHA agrees with this proposal and has amended the request to state the registered substance, only.

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: Pre-natal developmental toxicity study (test method: OECD TG 414) in a first species (rat or rabbit) by the oral route.

4. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species

Pre-natal developmental toxicity studies (test method OECD TG 414) on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation. However, as explained above in the section 'Grouping and read-across approach', your adaptation of the information requirement is rejected. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with rabbits or rats as a second species, depending on the species tested in the first pre-natal developmental toxicity study.
ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment*

(version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid, ECHA concludes that testing should be performed by the oral route.

In your comments on the draft decision, you propose to conduct a reproductive and developmental toxicity screening test (OECD TG 421) with Sodium cumene sulphonate (EC No. 239-854-6) prior to conducting the requested Pre-natal developmental toxicity studies. Should this "bridging infromation" confirm the assumed toxicity profile of the substance you propose to adapt the requests for an OECD TG 414 studies. If not you agree to conduct the OECD TG 414 studies. ECHA cannot currently assess if your proposed testing strategy would be acceptable. ECHA will evaluate your information after the deadline of this decision according to the specific rules of column 2 adaptations and adaptation(s) according to Annex XI. You also indicated that Sodium cumene sulphonate (EC No. 239-854-6) is the most appropriate substance to test since the sodium ion is ubiquitous in mammalian systems. ECHA agrees with this proposal and has amended the request to state the registered substance, only.

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: Pre-natal developmental toxicity study (test method: OECD TG 414) in a second species (rabbit or rat) by the oral route.

Notes for your consideration

You are reminded that before performing a pre-natal developmental toxicity study in a second species you must consider the specific adaptation possibilities of Annex X, Section 8.7., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species with other available information enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement.

5. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)

"Short-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex VII, Section 9.1.1. 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 the following four study records on analogue substances:

1. Key study on sodium xylene sulphonate according to EPA OTS 797.1300 (Aquatic Invertebrate Acute Toxicity Test, Freshwater Daphnids): [redacted], reliability 2.
2. Supporting study on sodium toluene sulphonate according to EU Method C.2 (Acute Toxicity for *Daphnia*): [redacted] reliability 2.
3. Supporting study on calcium xylene sulphonate according to EPA OTS 797.1300 (Aquatic Invertebrate Acute Toxicity Test, Freshwater Daphnids): [redacted] reliability 1.

4. Supporting study on sodium xylene sulphonate according to OECD Guideline 202 (*Daphnia sp.* Acute Immobilisation Test): [redacted], reliability 2.

However, as explained above in the section 'Grouping and read-across approach', your adaptation of the information requirement is rejected.

Furthermore, you have provided as supporting study a study record on the registered substance for an OECD Guideline 202 (*Daphnia sp.* Acute Immobilisation Test): [redacted] reliability 2.

However, this study, as well as the read-across study no. 4, do not provide the information required by Annex VII, Section 9.1.1., for the reasons described in the section 'Grouping and read-across approach'.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017) *Daphnia sp.* acute immobilisation test (test method EU C.2. / OECD TG 202) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.1.

In your comments on the draft decision you indicate that you will re-evaluate the available study with the registered substance ([redacted]. You agree to perform a new test only if this available study is not adequate to fulfil the current information requirement.

However, ECHA has already assessed this available study as not adequate for this decision. As explained in the section 'Grouping and read-across approach', the concentration tested in this study (i.e. 40.3 mg a.i./L) is below the threshold of 100 mg/L given in paragraph 24 of OECD TG 202. Therefore, as already indicated above, this available study with the registered substance cannot be used to fulfil the current information requirement.

In your comments on the draft decision you also indicate that Sodium cumene sulphonate (EC No. 239-854-6) is the most appropriate substance to test since the sodium ion is ubiquitous in the environment, which ECHA accepts and has amended the request to state the registered substance, only.

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: *Daphnia sp.* Acute immobilisation test, EU C.2./OECD TG 202).

6. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. 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 the following three study records:

1. Key study on sodium xylene sulphonate according to EPA OTS 797.1050 (Algal Toxicity, Tiers I and II[redacted], reliability 2.
2. Supporting study on sodium toluene sulphonate according to EU Method C.3 (Algal Inhibition test): [redacted], reliability 2.
3. Supporting study on calcium xylene sulphonate according to EPA OTS 797.1050 (Algal Toxicity, Tiers I and II): [redacted], reliability 1.

However, as explained above in the section 'Grouping and read-across approach', your adaptation of the information requirement is rejected. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

In your comments on the draft decision, you agree to conduct the requested study. You also indicate that Sodium cumene sulphonate (EC No. 239-854-6) is the most appropriate substance to test since the sodium ion is ubiquitous in the environment. ECHA agrees with this proposal and has amended the request to state the registered substance, only.

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: Algae growth inhibition test, EU C.3./OECD TG 201).

7. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

"Short-term toxicity testing on fish" is a standard information requirement as laid down in Annex VIII, Section 9.1.3. 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 the following two study records:

1. Key study on sodium xylene sulphonate equivalent or similar to EPA OTS 797.1400 (Fish Acute Toxicity Test): [redacted], reliability 2;
2. Supporting study on calcium xylene sulphonate according to EPA OTS 797.1400 (Fish Acute Toxicity Test): [redacted], reliability 1.

However, as explained above in the section 'Grouping and read-across approach', your adaptation of the information requirement is rejected. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017) fish acute toxicity test (test method EU C.1. / OECD TG 203) is the preferred test to cover the standard information requirement of Annex VIII, Section 9.1.3.

In your comments on the draft decision, you agree to conduct the requested study. You also indicate that Sodium cumene sulphonate (EC No. 239-854-6) is the most appropriate substance to test since the sodium ion is ubiquitous in the environment. ECHA agrees with this proposal and has amended the request to state the registered substance, only.

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: Fish, acute toxicity test (test method: EU C.1./OECD TG 203).

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

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.5., column 2. You provided the following justification for the adaptation: *"An environmental risk assessment has indicated that the members of the hydrotrope category do not pose a risk to the aquatic environment for all relevant uses. In Annex IX of Regulation (EC) No 1907/2006, it is laid down that chronic toxicity tests shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further. Since the chronic testing would not change the outcome of the environmental risk assessment no additional chronic testing on aquatic invertebrates appears to be justified. One chronic test on invertebrates is available (see RSS entry), but is considered of poor reliability. Use of this data, despite its unreliability would not change the outcome of the environmental risk assessment."*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.5., column 2. Firstly, as discussed in points 5-7 above, the acute aquatic toxicity information you have used as basis for PNEC derivation and the current Chemical Safety Assessment (CSA) for environment cannot be considered acceptable. Secondly, the ready biodegradability data available in the technical dossier cannot be considered reliable, as discussed in point 10. below. As a result, the exposure assessment based on the conclusion that the substance is ready biodegradable is currently not reliable. For these two reasons, the CSA including the exposure assessment and the risk characterisation sections cannot, with the available information, be used to adapt this information requirement.

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

Furthermore, you have provided a study record on the registered substance for long-term toxicity test on *Daphnia magna* (*"Long-term toxicity to aquatic invertebrates.002"*) with reliability 4. ECHA agrees that this read-across study is not reliable, as also described above

in the section 'Grouping and read-across approach'. Thus, it does not provide the information required by Annex IX, Section 9.1.5.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) *Daphnia magna* reproduction test (test method EU C.20. / OECD TG 211) is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5.

In your comments on the draft decision you propose a stepwise testing strategy for this endpoint and for long-term toxicity testing on fish (request 9).

You agree to complete first the requirements on short-term aquatic studies for the registered substance (requests 5-7). You also agree to complete the requirements on ready biodegradability (as discussed under point 10 below). Successively, you would update the CSA and determine whether the long-term *Daphnia* and the long-term fish (request 9) studies requested in this decision are needed.

If the CSA shows that further investigation of effects on aquatic organisms is required, you indicate that you will follow a stepwise approach for long-term aquatic toxicity testing.

You propose to perform first a long-term *Daphnia* study with "*representative substance(s)*" and, if the updated CSA still shows risk to the aquatic compartment, you will then perform also a long-term fish study with "*representative substance(s)*", which will be chosen based on an updated-read across justification after completing the requirements on short-term aquatic endpoints for the category members.

ECHA agrees that an Integrated Testing Strategy (ITS) can be used to determine the order of the studies to be performed and the necessity to conduct the long-term toxicity testing on aquatic invertebrates and on fish, as explained in the *Note for your consideration* below. However, ECHA notes the following issues with your proposed stepwise approach for long-term aquatic toxicity testing:

- First, while you propose to perform first a long-term *Daphnia* study, you do not consider if long-term testing should start with a long-term fish study. ECHA notes that, according to the ITS in ECHA Guidance Chapter R7b, Section R.7.8.5 and Figure R.7.8-4, if there is compelling evidence that fish is substantially more sensitive than other trophic levels, long-term testing should be performed with fish.
  Second, while based on the currently available information the read-across is not acceptable, ECHA acknowledges your intention to update the read-across for aquatic toxicity endpoints. However, as explained in section 'Grouping and read-across approach' above, ECHA cannot currently assess whether your proposal to test "*representative substance(s)*" and use read-across adaptations for the long-term aquatic toxicity endpoints would be acceptable. ECHA will evaluate your information after the deadline of this decision according to the specific rules of column 2 adaptations and adaptation(s) according to Annex XI.

In your comments on the draft decision, you also indicate that Sodium cumene sulphonate (EC No. 239-854-6) is the most appropriate substance to test since the sodium ion is

ubiquitous in the environment, which ECHA accepts and has amended the request to state the registered substance, only.

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

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

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. Adequate information on Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.), or Fish, short-term toxicity test on embryo and sac-fry stages (Annex IX, 9.1.6.2.), or Fish, juvenile growth test (Annex IX, 9.1.6.3.) needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a long-term toxicity on fish in the dossier that would meet the information requirement of Annex IX, Section 9.1.6.1 / 9.1.6.2 / 9.1.6.3.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.6., column 2. You provided the following justification for the adaptation: "*An environmental risk assessment has indicated that the members of the hydrotrope category do not pose a risk to the aquatic environment for all relevant uses. In Annex IX of Regulation (EC) No 1907/2006, it is laid down that chronic toxicity tests shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on fish. (..)*"

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.6., column 2. As already discussed in point 8. above, the risk characterisation is currently not reliable. Therefore, the CSA cannot be currently used to adapt the current information requirement.

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

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017) fish early-life stage (FELS) toxicity test (test method OECD TG 210), fish short-term toxicity test on embryo and sac-fry stages (test method EU C.15. / OECD TG 212) and fish juvenile growth test (test method EU C.14. / OECD TG 215) are the preferred tests to cover the standard information requirement of Annex IX, Section 9.1.6.

However, the FELS toxicity test according to OECD TG 210 is more sensitive than the fish, short-term toxicity test on embryo and sac-fry stages (test method EU C.15 / OECD TG 212), or the fish, juvenile growth test (test method EU C.14. / OECD TG 215), as it covers several life stages of the fish from the newly fertilized egg, through hatch to early stages of

growth (see ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b, Figure R.7.8-4).

Moreover, the FELS toxicity test is preferable for examining the potential toxic effects of substances which are expected to cause effects over a longer exposure period, or which require a longer exposure period of time to reach steady state (ECHA Guidance Chapter R7b, version 4.0, June 2017).

In your comments on the draft decision you propose a stepwise testing strategy for this endpoint and for long-term toxicity testing on aquatic invertebrates (request 8).

ECHA's response under point 8 also applies to this endpoint.

In your comments on the draft decision, you also indicate that Sodium cumene sulphonate (EC No. 239-854-6) is the most appropriate substance to test since the sodium ion is ubiquitous in the environment, which ECHA accepts and has amended the request to state the registered substance, only.

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

Note for your consideration for requests 5-9

Before conducting the tests requested above under points 8. and 9., you shall consult the ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Section R.7.8.5 to determine the necessity to conduct the long-term toxicity testing on aquatic invertebrates and on fish.

Concerning the order of studies to be conducted, you may first complete the requirements on short-term aquatic studies requested under points 5. to 7. in this decision, as well as on ready biodegradability requested under point 10. in this decision, and subsequently update the CSA according to Annex I of the REACH Regulation.

If you come to the conclusion that no further investigation of chronic effects on aquatic organisms is required, you shall update your technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex IX, 9.1.5 and 9.1.6. taking into account the new data generated by the short-term aquatic studies requested by the present decision and exposure assessment and risk characterisation.

On the other hand, if after the update of the CSA you come to the conclusion that the long-term toxicity tests are still required to refine the risk assessment, you should further consider the Integrated Testing Strategy (ITS) for aquatic toxicity as described in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4). According to the ITS, if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially less sensitive than other trophic levels (i.e. fish, invertebrates, algae), long-term studies may be required on both fish and invertebrates. In such case, according to the ITS, the long-term *Daphnia* study is to be conducted first. If based on the results of the

long-term *Daphnia* study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.

10. **Robust study summary (RSS) for [redacted], ready biodegradability (Annex VII, Section 9.2.1.1.);**

    OR

    Ready biodegradability study (Annex VII, Section 9.2.1.1.)

"Ready biodegradability" is a standard information requirement as laid down in Annex VII, section 9.2.1.1. 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.

Furthermore, pursuant to Article 10 (a)(vii) and Annex I, Section 3.1.5. if there are several studies addressing the same effect, then, the study or studies giving rise to the highest concern shall be used to draw the conclusion and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust study summaries will be required of all key data used in the hazard assessment.

You have provided the following seven study summaries to fulfill the Annex VII section 9.2.1.1. information requirement of Ready biodegradability (IUCLID section 5.2.1):

1. Key study on sodium toluene sulphonate, according to OECD Guideline 301B (Ready Biodegradability: CO2 Evolution Test): [redacted], reliability 1, GLP, result: 99.8% degradation after 28d.
2. Supporting study on the registered substance according to OECD Guideline 301D (Ready Biodegradability: Closed Bottle Test): [redacted], reliability 2, GLP not specified, result: 50% degradation after 28d.
3. Supporting study on the registered substance according to OECD Guideline 301B (Ready Biodegradability: CO2 Evolution Test): [redacted], reliability 1, GLP, result: >100% degradation after 28d.
4. Supporting study on calcium (xylenes and 4-ethylbenzene) sulphonate according to OECD Guideline 301B (Ready Biodegradability: CO2 Evolution Test): [redacted], reliability 1, GLP, result: 69-87% degradation after 29d.
5. Supporting study on sodium (xylenes and 4-ethylbenzene) sulphonate according to OECD Guideline 301 D (Ready Biodegradability: Closed Bottle Test): [redacted] reliability 2, GLP not specified, result: 40% degradation after 28d.
6. Supporting study on sodium (xylenes and 4-ethylbenzene) sulphonate according to OECD Guideline 301B (Ready Biodegradability: CO2 Evolution Test): [redacted] reliability 2, GLP not specified, result: 86-88% degradation after 28d.
7. Supporting study on sodium (xylenes and 4-ethylbenzene) sulphonate according to OECD Guideline 301B (Ready Biodegradability: CO2 Evolution Test): [redacted]

[redacted] reliability 1, GLP, result: 83-85% degradation after 28d.

ECHA notes that you have sought to adapt the information requirement for ready biodegradability according to Annex XI, Section 1.5. of the REACH Regulation by providing study no 1 above as the key study. However, as explained above in the section 'Grouping and read-across approach', your adaptation of the information requirement is rejected.

For the same reasons, also the supporting studies no 4 to 7 on (xylenes and 4-ethylbenzene) sulphonates cannot be used to adapt the information requirement for ready biodegradability according to Annex XI, Section 1.5. of the REACH Regulation. Furthermore, as described below, studies no 4 to 7 do not provide the information required by Annex VII, Section 9.2.1.1., because the information reported is insufficient to make an independent assessment of the study (study no 5), or they are not adequate (studies no 4, 6-7).

Regarding the supporting studies no 2 and 3 on the registered substance as described below, they do not provide the information required by Annex VII, Section 9.2.1.1., because the information reported is insufficient to make an independent assessment of the study (study no 2), or they are not adequate (study no 3).

Specifically, ECHA has identified the following issues regarding the provided studies:

a) Studies not adequate due to significant deviations from standard test guidelines and due to missing information

For studies no 3-4 and no 6-7 ECHA has identified the following deficiencies:

- Adaptation of the inoculum

  According to par. 18 of OECD TG 301, the inoculum used should not be pre-adapted to the test substance. For studies no 3 and 7, you report "adaptation not specified" for the inoculum, but you indicate that the inoculum used in these studies was acclimated in SCAS units for 9 days. ECHA considered this treatment as a not acceptable deviation from the requirements of OECD TG 301, as also explained in ECHA *Guidance on information requirements and chemical safety assessment*, Chapter R.7b (version 4.0, June 2017) Section R.7.9.4.1. Therefore, studies no 3 and no 7 cannot be considered adequate to conclude on this endpoint.

- No duplicates

  According to par. 12 of OECD TG 301, determinations should be carried out at least in duplicate. However, in studies no 3 and no 6 only one flask was used per test substance concentration. ECHA considers that this a significant deviation from OECD TG 301, also because results in replicates are needed to verify the validity of the ready biodegradability tests as described in par. 24 of OECD TG 301. Therefore, studies no 3 and 6 cannot be considered adequate to conclude on this endpoint.

- Concentration of inoculum

The inoculum concentrations of studies no 4 and no 6 are not compliant with the test conditions specified in Table 2 of OECD TG 301, since you report that the cell concentration was "*5.2 x 10-7*" cfu/mL in study 4 and "*10x8 germs viable*"/mL in study 6, while it should be between 10^7 and 10^8 cells/L. ECHA considers these inoculum concentrations as a significant deviation from the requirements of OECD TG 301, and you have not explained how this deviation might have affected the results. Therefore, studies no 4 and 6 cannot be considered adequate to conclude on this endpoint.

- Missing information to assess the validity and reliability of the study

ECHA notes further that for studies no 3-4 and no 6-7 you have not provided all information required in paragraph 27 of the OECD TG 301 and in ECHA's Practical Guide 3 "*How to report robust study summaries*". In particular, the following information is missing:

- Detailed description of the test substance
  For all mentioned studies, composition of the test material is not provided, hence it is not possible to verify whether the test material is representative of the registered substance.
- Detailed description of the inoculum
  You have not specified whether the inoculum was pre-adapted in studies no 4 and 6, and you have not provided information on inoculum concentration in studies no 3 and 7. In the absence of this information, it is not possible to verify whether the test conditions would comply with the requirement of par. 18 of OECD TG 301 regarding inoculum adaptation and of Table 2 of OECD TG 301 regarding inoculum concentration.
- Number of replicates per test substance concentration
  For study no 7 you have not reported the number of flasks per concentration, hence ECHA cannot verify whether it would comply with the requirements of par. 12 of OECD TG 301.
- Any deviations in the standard test protocols
- A clear reporting of the test results including all raw data in a tabular form
  In the absence of this information, ECHA cannot verify that the validity critieria, as defined in paragraphs 24 and 25 of OECD TG 301, have been fulfilled.

Due to the deficiencies listed above, ECHA concludes that studies no 3-4 and no 6-7 are not adequate and hence cannot be used to conclude on this endpoint nor to adapt the standard information requirement according to Annex XI, Section 1.5..

b) Insufficient information provided to assess the studies

Under Article 3(28) of the REACH Regulation, a Robust study summary "*means 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 minimising the need to consult the full study report*".

Specifically, for studies no 2 (on the registered substance) and no 5 (on (xylenes and 4-ethylbenzene) sulphonate), ECHA notes that, contrary to Article 3(28) of the REACH Regulation, the information provided in the robust study summary is insufficient to allow an independent assessment of these studies.

In this regard, ECHA notes that the Robust study summaries do not include critical information required in the OECD TG 301 and in ECHA's Practical Guide 3 "*How to report robust study summaries*", which is needed to assess the validity and reliability of the studies. This critical information concerns in particular:

- Details on the test substance (e.g. composition);
- Details on inoculum (concentration and any pre-conditioning treatment);
- Information on the test design as specified in the OECD TG 301 and any deviations in the standard test protocols;
- clear reporting of the test results (e.g. all raw data in a tabular form).

Due to the absence of this critical information, the robust study summaries of studies no 2 and 5 cannot be relied on for an independent assessment of the properties of the registered substance. As a consequence, while as explained above study no 5 on the analogue substance (xylenes and 4-ethylbenzene) sulphonate) cannot be used to adapt the information requirement according to Annex XI, Section 1.5., for study no 2 it cannot be established whether the information requirement is met.

Conclusions

In conclusion, 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.

Furthermore, ECHA notes that you have considered the registered substance readily biodegradable in your chemical safety assessment (CSA). ECHA considers that reliable information is needed for the risk assessment of the registered substance.
In your comments on the draft decision you agree to complete the RSS for this endpoint to allow an independent assessment. You indicate that you aim to complete the RSS for the study [redacted] with the missing critical information and to verify that the available study is reliable and adequate. If this is not the case, you agree to perform a new study. ECHA will evaluate your information after the deadline of this decision according to the specific rules of column 2 adaptations and adaptation(s) according to Annex XI. In your comments on the draft decision, you also indicate that Sodium cumene sulphonate (EC No. 239-854-6) is the most appropriate substance to test since the sodium ion is ubiquitous in the environment. ECHA agrees with this proposal and has amended the request to state the registered substance, only.

In order to allow an independent assessment of the study no 2 submitted,, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to provide complete robust study summary for the study: [redacted] with the above missing information for the study.

Alternatively, if you cannot submit a complete RSS or the RSS indicates that the study is not reliable as per the criteria indicated above and/or not adequate to fulfil the information requirement, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance:

> Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: DOC die-away test, OECD TG 301A) or

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: CO2 evolution test, OECD TG 301B) or

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: MITI test (I), OECD TG 301C) or

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Closed bottle test, OECD TG 301D) or

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Modified OECD screening test, OECD TG 301E) or

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Manometric respirometry test, OECD TG 301F) or

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Ready biodegradability – CO2 in sealed vessels (headspace test), OECD TG 310.

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 06/09/2018.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

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

ECHA took into account your comments and amended all the request(s) to state testing with the registered substance.

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 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 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.

4. If the required tests are conducted with an analogue substance in the context of a read-across approach, the identity of the test material used to perform the test should be specified in line with ECHA's Practical Guide on "How to use alternatives to animal testing to fulfil your information requirements" (chapter 4.4). This is required to show that the test material is representative of the analogue substance identified in the read-across approach and used to predict the properties of the registered substance.