~~Confidential~~

Helsinki, 28 May 2021

Addressee
Registrant of JS_939-154-7 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
17/05/2013

Registered substance subject to this decision ("the Substance")
Substance name: Reaction mass of sodium 4-hydroxybenzenesulfonate and disodium 4-hydroxybenzene-1,3-disulfonate and sodium sulfate
List number: 939-154-7
CAS number: NS

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***5 June 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)
4. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: OECD TG 301B/C/D/F or OECD TG 310)

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

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)
2. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)
3. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or 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)
5. Adsorption/ desorption screening (Annex VIII, Section 9.3.1.; test method: OECD TG 106)

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

1. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats
2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)
3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)
4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

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 IX 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, VIII and IX to REACH, for registration at 100-1000 tpa.

How to comply with your information requirements

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

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

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

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

Authorised[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix on Reasons common to several requests

1. Assessment of your read-across approach under Annex XI, Section 1.5 for the category approach 'Aromatic sulphonic acids and salts'

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 cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

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.

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.

A. Scope of the grouping

1. Description of the grouping

In your registration dossier you have formed a group (category) of 'Aromatic sulphonic acids and salts'. You have not provided any justification for the predictions of the toxicological properties listed above.

For the purpose of this decision, the following substance names are used regarding the group members:

[1] sodium 4-methylbenzenesulfonate, (also known as sodium toluene-4-sulphonate) (EC number 211-522-5)
[2] sodium cumene sulphonate (EC number 248-983-7)
[3] calcium xylenesulphonate (EC number 248-829-9)
[4] sodium 3,4-dimethylbenzenesulfonate (EC number 215-090-9)
[5] sodium xylene sulphonate (EC number 215-090-9)
[6] p-toluene sulphonic acid (EC number 203-180-0)
[7] benzenesulfonic acid (EC number 202-638-7)
[8] sodium toluene sulphonate (EC number 235-088-1)

You have not provided any reasoning for the grouping of the substances.

2. Assessment of the grouping

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

i. Applicability domain of the category

A category (grouping) hypothesis must 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*" (ECHA Guidance 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*" (ECHA Guidance R.6.2.1.2). Therefore, to reliably predict properties within a category the applicability domain must 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.

You have not provided a description of the applicability domain of the substances covered by the category approach.

As you have not provided unambiguous inclusion/exclusion criteria, it is not possible to identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological and/or ecotoxicological properties within which you consider that reliable estimations can be made for the category members.

ii. Characterisation of the group members

Annex XI, Section 1.5 of REACH 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*". ECHA Guidance clarifies that "*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 (ECHA Guidance 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.

As already explained above, you have not defined the applicability domain of the category. Further, you have not provided compositional information for the members of your category including a comprehensive description of their purity profile and of the presence of impurities.

Without the compositional information for the category members (and a definition of the applicability domain of the category), the category membership cannot be evaluated.

B. Predictions for toxicological properties

You have not provided any specific reasoning for the prediction of the toxicological properties listed above.

In the absence of any specific reasoning, ECHA considers 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 gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- p-toluene sulphonic acid (EC number 203-180-0)

- benzenesulfonic acid (EC number 202-638-7)

In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- p-toluene sulphonic acid (EC number 203-180-0)
- sodium toluene sulphonate (EC number 235-088-1)

Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- sodium toluene sulphonate (EC number 235-088-1)

Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- calcium xylenesulphonate (EC number 248-829-9)

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

1. Supporting information

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*" (ECHA Guidance 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.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar category members cause the same type of effects. In this context, supporting information must include bridging studies of comparable design and duration for the category members and the Substance.

The data set reported in the technical dossier does not include any bridging studies 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 enough supporting information to strengthen the rationale for the read-across. This issue equally applies to predictions of toxicological properties, aquatic toxicity and environmental fate properties.

2. Data density

Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances".* ECHA Guidance R.6.2.1.5 clarifies that one of the factors in determining the robustness of a category is the density and distribution of the available data across the category. To identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the category members must be available.

For each toxicological property, you have provided some information on a single or only few category members. Furthermore, as explained below under "*Adequacy and reliability of source studies*" (see issue 3 below), we have identified several shortcomings with some of the studies you provided on the selected category members.

Therefore, the information provided is not sufficient to conclude that toxicological properties are likely to be similar within the category.

3. Adequacy and reliability of source studies

Under Annex XI, Section 1.5., if grouping concept is applied then in all cases, the results 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.

We have identified several shortcomings with some of the studies you provided on the selected category members. These deficiencies are addressed under the corresponding information requirements in Appendices A to C.

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

As detailed above, you have not established that relevant properties of the Substance can be predicted from data on the category members. 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.

In your comments on the draft decision, you agreed to re-evaluate the read-across approach when information on the substance is not available. You intend to update your registration dossier accordingly.

2. Assessment of your read-across approach under Annex XI, Section 1.5 for the analogue approach with disodium sulphate (EC number 231-820-9)

In addition to the category approach described above, you also seek to adapt the information requirements for the following standard information requirements by applying read-across approaches 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 8.4.3.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

The general principles of read-across adaptations already described in section 1 above equally apply to this section.

A. Predictions for toxicological properties

You have not provided any reasoning for the prediction of toxicological properties

You read across between the structurally similar substance, disodium sulphate (EC number 231-820-9) as source substance and the Substance as target substance.

ECHA notes that this analogue substance represents the main constituent of the Substance (i.e. between 50 and 70 % (w/w)). 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.

ECHA notes the following issues with regards to predictions for repeated dose toxicity and aquatic toxicity properties:

1. Absence of read-across documentation

Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide a justification for the read-across including a hypothesis, explanation of the rationale for the prediction of properties and robust study summary(ies) of the source study(ies) (ECHA Guidance R.6.2.6.1).

You have provided studies conducted with disodium sulphate in order to comply with the REACH information requirements. You have not provided documentation as to why this information is relevant for your Substance.

In the absence of such documentation, ECHA cannot verify that the properties of your Substance can be predicted from the data on the source substance(s).

2. Supporting information

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*" (ECHA Guidance 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 the source substance.

The selected analogue substance is an inorganic salt corresponding to the main constituent of the Substance. In this context, supporting information must include relevant and reliable information on the properties of the non-common constituents. The impact of exposure to these non-common compounds on the prediction of properties of the Substance needs to be assessed to ensure that a reliable prediction can be made.

You have not provided any information on the properties of the non-common constituents for the endpoints listed above.

In the absence of such information, you have not established that a reliable prediction of the property under consideration of the Substance can be derived on the basis of your read-across hypothesis. Therefore, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

B. Conclusions on the 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, disodium sulphate. 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.

In your comments on the draft decision, you agreed to re-evaluate the read-across approach when information on the substance is not available. You intend to update your registration dossier accordingly.

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

- You have adapted the following information requirements according to Annex XI, Section 1.2. of REACH (weight of evidence):Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

In support of your adaptation, you have provided the following sources of information:

a. a read-across adaptation based on an analogue approach with disodium sulphate (EC number 231-820-9);
b. a read-across adaptation based on a category approach with a group of 'Aromatic sulphonic acids and salts'.

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.4.4, a weight of evidence adaptation involves an assessment of the relative values/weights of 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 of the information for the given regulatory information requirement. Subsequently, relevance, reliability, 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 information requirement listed above, 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.

Deficiencies specific to certain information requirements are addressed under the respective sections in the Appendices below. However, the following deficiency is common to all information requirements for which you invoked a weight of evidence adaptation:

Reliability of the read across approaches

Section 1 and 2 of the present Appendix identifies deficiencies of the grouping and read across approaches used in your dossier. These findings apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptations. These deficiencies affect significantly the reliability of the sources of information relating to analogue substances.

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 adapted this information requirement under Annex XI, Section 1.5 (read-across). In support of your adaptation, you have provided the following information:

1. an *in vitro* gene mutation study in bacteria (OECD TG 471, key study) on p-toluene sulfonic acid (EC number 203-180-0) ([redacted], 1988);
2. an *in vitro* gene mutation study in bacteria (non guideline study, key study) on disodium sulphate (EC number 231-820-9) (Gocke *et al.*, 1981);
3. a publication reporting information on *in vitro* gene mutation in bacteria on benzenesulfonic acid (EC number 202-638-7) ([redacted] 1998).

We have assessed this information and identified the following issues:

A. Rejected read-across adaptations

As explained under the appendix on 'Reasons common to several requests', your read-across adaptations under Annex XI, Section 1.5. are rejected as you have not established that relevant properties of the Substance can be predicted using either data on the analogue disodium sulphate or data on the members of the 'Aromatic sulphonic acids and salts' category.

B. The studies provided are also not in line with the requirements in OECD TG 471 (1997)

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[2] (1997). Some of the key specifications of this test guideline include:

a) the test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101);
b) 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 dose must correspond to 5 mg/plate or 5 ml/plate;
c) at least 5 doses must be evaluated, in each test condition;
d) the number of revertant colonies per plate for the concurrent negative control must be inside the historical control range of the laboratory;
e) the mean number of revertant colonies per plate must be reported for the treated doses and the controls.

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

a) the results for the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) in studies 1., 2. and 3.;
b) a maximum dose of 5 mg/plate or 5 ml/plate or that induced a reduction in the number of revertant colonies per plate compared to the negative control in study 2.;
c) the number of doses in each test condition in studies 2. and 3.;
d) reporting on the negative control with a number of revertant colonies per plate demonstrating it is inside the historical control range of the laboratory in studies 1., 2. and 3.;
e) reporting on the number of revertant colonies per plate for the treated doses and the

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

controls in studies 1., 2. and 3.

Therefore, none of the studies listed above meets the information requirement.

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision, you explain that you intend to adapt this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across approach') using information on the similar substance Reaction mass of 4-hydroxybenzene-1,3-disulphonic acid and 4-hydroxybenzenesulphonic acid and sulphuric acid and water (EC number 938-815-7). You specify that the study on the similar substance will be generated in the context of an ongoing compliance check for that substance. You have provided a brief description of the proposed read-across approach including compositional information on the target and source substance, some basic physico-chemical properties and the outcome from structural alert profilers form the QSAR Toolbox v.4.4.

In the absence of a comprehensive read-across justification document and of the results of the study on the analogue substance, ECHA is not in a position to make an assessment of the validity of the proposed adaptation.

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 an adaptation under Annex XI, Section 1.2. (weight of evidence). In support of your adaptation, you provided the following sources of information:

1. a short-term toxicity study on aquatic invertebrates according to OECD TG 202 with benzenesulfonic acid (EC number 202-638-7) ([redacted] 2005);
2. a short-term toxicity study on aquatic invertebrates according to OECD TG 202 with p-toluene sulphonic acid (EC number 203-180-0) ([redacted] 2010);
3. a short-term toxicity study on aquatic invertebrates according to OECD TG 202 with benzenesulfonic acid (EC number 202-638-7) ([redacted], 1995);
4. a non-guideline short-term toxicity study on aquatic invertebrates with disodium sulphate (EC number 231-820-9) (Warne & Schifko, 1999);
5. a short-term toxicity study on aquatic invertebrates according to EPA/600/4-90/ 027 with disodium sulphate (EC number 231-820-9) (Mount *et al.*, 1997).

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.

To fulfil the information requirement on short-term toxicity study on aquatic invertebrates, normally a study performed according to OECD TG 202 must be provided. OECD TG 202 investigates the following: the concentration of the test material leading to the immobilisation of 50% of daphnids at the end of the test.

The sources of information 1. to 5. provide relevant information on immobilisation of daphnids.

However, the reliability of these sources of information is significantly affected by the following deficiencies:

A. *Rejected read-across adaptations*

The sub-sections 1 and 2 of the appendix on 'Reasons common to several requests' detail deficiencies with your category approach for 'Aromatic sulphonic acids and salts' and your analogue approach for disodium sulphate (EC number 231-820-9). As explained under section 3 of the appendix on 'Reasons common to several requests', these findings apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptations.

In addition to the deficiencies referred to above, we note that you have not provided any reasoning for the prediction of short-term toxicity on aquatic invertebrates using the category approach for 'Aromatic sulphonic acids and salts'. However, you consider that:

- *"an environmental risk assessment has indicated that the members of the Aromatic Sulphonic Salt category do not pose a risk to the aquatic environment for all relevant uses"*;
- *"the disulphonated component is expected not to have an impact* [...]".

ECHA understands that you predict the properties of the Substance using a category 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:

- p-toluene sulphonic acid (EC number 203-180-0)
- benzenesulfonic acid (EC number 202-638-7)

Annex XI, Section 1.5. provides that *"substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances"*. ECHA Guidance R.6.2.1.5 clarifies that one of the factors in determining the robustness of a category is the density and distribution of the available data across the category. To identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the category members must be available.

However, as explained under issue B. below, the information on p-toluene sulphonic acid (EC number 203-180-0) does not meet the information requirement.

As you have only provided reliable information from a single category member, this information is not sufficient to conclude that short-term toxicity on aquatic invertebrates is likely to be similar within the category.

On the basis of the above, you have not established that relevant properties of the Substance can be predicted using either data on the analogue disodium sulphate or data on the members of the 'Aromatic sulphonic acids and salts' category. Therefore, the reliability of such information in support of your weight of evidence adaptation under Annex XI, Section 1.2 is considered low.

B. *The source of information 2. has low reliability:*

To inform on short-term toxicity on aquatic invertebrates, a study must provide equivalent information to study described in the OECD TG 202 test method. Therefore, the following key specifications are normally expected to be met:

Technical specifications impacting the sensitivity/reliability of the test

- the test duration is 48 hours or longer. However, in study 2., the exposure duration was only 24 hours;

Characterisation of exposure

- 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. However, in study 2., no analytical monitoring of exposure was conducted.

Due to these significant deficiencies, the source of information 2. does not provide an adequate and reliable coverage of the key parameter addressed in OECD TG 202. Therefore, the reliability of such information in support of your weight of evidence adaptation under Annex XI, Section 1.2 is considered low.

Conclusion on your weight of evidence adaptation:

Taken together, even if these sources of information provide information on short-term toxicity on aquatic invertebrates, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

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

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision, you explain that you intend to adapt this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across approach') using information on the similar substance Reaction mass of 4-hydroxybenzene-1,3-disulphonic acid and 4-hydroxybenzenesulphonic acid and sulphuric acid and water (EC number 938-815-7). You specify that the study on the similar substance will be generated in the context of an ongoing compliance check for that substance. You have provided a brief description of the proposed read-across approach including compositional information on the target and source substance, some basic physico-chemical properties and the outcome from structural alert profilers form the QSAR Toolbox v.4.4.

In the absence of a comprehensive read-across justification document and of the results of the study on the analogue substance, ECHA is not in a position to make an assessment of the validity of the proposed adaptation.

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 an adaptation under Annex XI, Section 1.2. (weight of evidence). In support of your adaptation, you provided the following sources of information:

1. a growth inhibition study on algae according to EPA OTS 797.1050 with sodium xylene sulphonate (EC number 215-090-9) ([redacted], 1993)
2. a growth inhibition study on algae according to EU Method C.3 with sodium 4-methylbenzene-sulfonate (EC number 211-522-5) ([redacted], 1995)
3. a growth inhibition study on algae according to EPA OTS 797.1050 with calcium xylenesulphonate (EC number 248-829-9) ([redacted], 1994)

4. an extract from the Database U.S. EPA ECOTOX (Version 4, 2013) on disodium sulphate (EC number 231-820-9)
5. a non-guideline growth inhibition study on algae test with disodium sulphate (EC number 231-820-9) (Soucek, 2007)
6. a non-guideline growth inhibition study on algae with disodium sulphate (EC number 231-820-9) (Patrick *et al.*, 1968)

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.

To fulfil the information requirement on growth inhibition on aquatic plants, normally a growth inhibition study on algae performed according to OECD TG 201 must be provided. OECD TG 201 investigates the following: 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.

The sources of information 1. to 5. provide relevant information on the above key investigations.

However, the reliability of these sources of information is significantly affected by the following deficiencies:

A. *Rejected read-across adaptations*

The sub-sections 1 and 2 of the appendix on 'Reasons common to several requests' detail deficiencies with your category approach for 'Aromatic sulphonic acids and salts' and your analogue approach for disodium sulphate (EC 231-820-9). As explained under section 3 of the appendix on 'Reasons common to several requests', these findings apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptations.

In addition to the deficiencies referred to above, we note that you have not provided any reasoning for the prediction of growth inhibition on algae using the category approach for 'Aromatic sulphonic acids and salts'. However, you consider that:

- "*an environmental risk assessment has indicated that the members of the Aromatic Sulphonic Salt category do not pose a risk to the aquatic environment for all relevant uses*";
- "*the disulphonated component is expected not to have an impact* [...]".

ECHA understands that you predict the properties of the Substance using a category 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:

- sodium xylene sulphonate (EC number 215-090-9)
- sodium 4-methylbenzenesulfonate (EC number 211-522-5)
- calcium xylenesulphonate (EC number 248-829-9)

Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances".* ECHA Guidance R.6.2.1.5 clarifies that one of the factors in determining the robustness of a category is the density and distribution of the available data across the category. To identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the category members must be available.

However, as explained under issue B. below, the identity of the test material used in the provided studies is unclear. Furthermore, as explained under issue C. below, the information on sodium xylene sulphonate (EC number 215-090-9; study 1. above) and calcium xylenesulphonate (EC number 248-829-9; study 3. above) does not meet the information requirement. Therefore, the information provided is not adequate to conclude that growth inhibition on algae is likely to be similar within the category.

On the basis of the above, you have not established that relevant properties of the Substance can be predicted using either data on the analogue disodium sulphate or data on the members of the 'Aromatic sulphonic acids and salts' category. Therefore, the reliability of such information in support of your weight of evidence adaptation under Annex XI, Section 1.2 is considered low.

B. The identity of the test material in studies 1. to 3. is unclear

For studies 1. to 3., you report that the purity of the test material ranged from 31.2% to 42.8% depending on the study. You have not provided further information, including composition and presence of impurities in the corresponding test materials.

In the absence of composition information, the identity, composition and presence of impurities of the test material cannot be assessed. Therefore, the information provided is rejected.

C. The sources of information 1. and 3. have low reliability:

To inform on growth inhibition on algae, a study must provide equivalent information to study described in the OECD TG 201 test method. Therefore, the following key specifications are normally expected to be met:

Validity criteria and reporting of the methodology and results

- exponential growth in the control cultures is observed over the entire duration of the test;
- at least 16-fold increase in biomass is observed in the control cultures by the end of the test;
- the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%;
- the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures is ≤ 7%.
- the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

For studies 1 and 3, tabulated data on the algal biomass determined daily for each treatment group and control are not reported. Therefore, it is not possible to verify whether validity criteria consistent with the requirements of OECD TG 201 were met for these studies.

Characterisation of exposure

- 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 EC_{50}.

However, for study 1, you reported that no analytical monitoring of exposure was conducted. In the absence of this information, you have not demonstrated that exposure was satisfactorily maintained over the duration of the test and that effect concentrations can be reliably expressed based on nominal concentrations.

Due to these significant deficiencies, the sources of information 1. and 3. do not provide an adequate and reliable coverage of the key parameter addressed in OECD TG 201. Therefore, the reliability of such information in support of your weight of evidence adaptation under Annex XI, Section 1.2 is considered low.

Conclusion on your weight of evidence adaptation:

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

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

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision, you explain that you intend to adapt this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across approach') using information on the similar substance Reaction mass of 4-hydroxybenzene-1,3-disulphonic acid and 4-hydroxybenzenesulphonic acid and sulphuric acid and water (EC number 938-815-7). You specify that the study on the similar substance will be generated in the context of an ongoing compliance check for that substance. You have provided a brief description of the proposed read-across approach including compositional information on the target and source substance, some basic physico-chemical properties and the outcome from structural alert profilers form the QSAR Toolbox v.4.4.

In the absence of a comprehensive read-across justification document and of the results of the study on the analogue substance, ECHA is not in a position to make an assessment of the validity of the proposed adaptation.

4. Ready biodegradability

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

You have provided an adaptation under Annex XI, Section 1.2. (weight of evidence) supported by the following sources of information:

1. a ready biodegradability study according to OECD TG 301D with sodium cumene sulphonate (EC number 248-983-7) ([redacted] 1995);

2. a ready biodegradability study according to OECD TG 301D with sodium 3,4-dimethylbenzenesulfonate (EC number 215-090-9)) ([redacted], 1995);
3. a ready biodegradability study according to OECD TG 301B with calcium xylene sulphonate (EC number 248-829-9) ([redacted], 1994);
4. a ready biodegradability study according to OECD TG 301B with sodium cumene sulphonate (EC number 248-983-7) ([redacted], 1994);
5. a ready biodegradability study according to OECD TG 301B with sodium xylene sulphonate (EC number 215-090-9) ([redacted], 1993);
6. a ready biodegradability study according to OECD TG 301B with sodium 4-methylbenzenesulfonate (EC number 211-522-5) ([redacted], 2004).

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.

To fulfil the information requirement on ready biodegradability, normally a study performed according to OECD TG 301 or 310 must be provided. OECD TG 301 or 310 investigate the following: the ultimate aerobic biodegradation (as measured by parameters such as DOC removal, CO_2 production and oxygen uptake) of the test material under low inoculum concentration (with a non-adapted inoculum representing a mixed bacterial community) and measured at sufficiently frequent intervals to allow the identification of the beginning and end of biodegradation.

The sources of information 1. to 6. provide relevant information on the above key investigations.

However, the reliability of these sources of information is significantly affected by the following deficiencies:

A. Rejected read-across adaptations

The sub-section 1 of the appendix on 'Reasons common to several requests' detail deficiencies with your category approach for 'Aromatic sulphonic acids and salts'. As explained under section 3 of the appendix on 'Reasons common to several requests', these findings apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptations.

For the prediction of ready biodegradability, we note that you have provided the following reasoning for the prediction of environmental fate properties:

- *"the aromatic sulphonic salts are soluble in water and are neither sorptive, nor volatile, nor bioaccumulative"* and *"they should partition primarily to the water compartment"*;
- *"these substances completely ionise in water even at low pH"*;
- *"these substances are neither hydrolysable nor photolysable"*;
- *"the aromatic sulphonic salts as a category are not persistent"*.

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:

- sodium 4-methylbenzenesulfonate (EC number 211-522-5)

- sodium cumene sulphonate (EC number 248-983-7)
- calcium xylene sulphonate (EC number 248-829-9)
- sodium 3,4-dimethylbenzenesulfonate (EC number 215-090-9)
- sodium xylene sulphonate (EC number 215-090-9)

ECHA Guidance R.6.2.2.1.f indicates that "*it is important to provide supporting information to strengthen the rationale for the read-across*". 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 category members. The observation of differences in the environmental fate properties between the source substances and the Substance would contradict the hypothesis that the properties of the Substance can be predicted from the data on the similar substances. An explanation why such differences do not affect the read-across hypothesis needs to be provided and supported by scientific evidence.

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).

Without considerations of the shortcomings in the studies provided on the category members (See issues B. and C. below), the study provided on sodium cumene sulphonate (EC number 248-983-7) shows that biodegradation did not reach 60% biodegradation by the end of the test (i.e. 28 days). The study on calcium xylene sulphonate (EC number 248-829-9) indicates that these substance did not meet the 10-d window criteria. Finally, for a number of other studies, the 10d-window criteria cannot be verified.

The available set of data on the category members indicates differences in their environmental fate properties. This contradicts your read-across hypothesis whereby the structurally similar category members have similar properties. Therefore, you have not demonstrated and justified that the properties of the category members are likely to be similar despite the observation of these differences.

On the basis of the above, you have not established that relevant properties of the Substance can be predicted using either data on the members of the 'Aromatic sulphonic acids and salts' category. Therefore, the reliability of such information in support of your weight of evidence adaptation under Annex XI, Section 1.2 is considered low.

B. The identity of the test material in studies 1. to 3. is unclear

For studies 1. and 3., you report that the purity of the test material was [redacted] and [redacted] respectively without further information, including composition and presence of impurities. For studies 2, 4 and 5, you have not provided identification information of the test material (i.e. CAS and/or EC numbers) and no information on composition.

In the absence of composition information, the identity, composition and presence of impurities of the test material cannot be assessed. Therefore, the information provided is rejected.

C. The sources of information 1. and 3. have low reliability:

To inform on ready biodegradability, a study must provide equivalent information to a ready biodegradability study described in any of the OECD TG 301 or 310 test methods. Therefore, for a study claimed to be conducted according to OECD TG 301, the following key specifications are normally expected to be met:

Validity criteria and reporting

- The difference of extremes of replicate values of the removal of the test material at the plateau, at the end of the test or, if appropriate, at the end of the 10-d window is ≤ 20%.
- For a study according to OECD TG 301B, the inorganic carbon content (IC) of the test material suspension in the mineral medium at the beginning of the test is < 5% of the total carbon (TC);
- For a study according to OECD TG 301D, the oxygen depletion in the inoculum blank is ≤ 1.5 mg dissolved O_2/L after 28 days and the residual concentration of oxygen in the test bottles is ≥ 0.5 mg O_2/L at any time;
- The results of measurements at each sampling point in each replicate is reported in a tabular form;

  You have not reported the results of measurements at each sampling point in each replicate is reported in a tabular form for any of the studies. Therefore, it is not possible to verify whether or not validity criteria consistent with the corresponding test guideline were met.

Technical specifications impacting the sensitivity/reliability of the test

- The inoculum is not be pre-adapted to the test material;

  For studies 1. to 5., you report that it is not specified if the inoculum was adapted to the test material.

- For a study according to OECD TG 301B, the concentration of the inoculum is set to reach a bacterial cell density of 10^7 to 10^8 cells/L in the test vessel. For a study according to OECD TG 301D, the concentration of the inoculum is set to reach a bacterial cell density of 10^4 to 10^6 cells/L in the test vessel;

  However, no information is provided on the concentration of the inoculum at the beginning of the test in cells/L for studies 1., 2. and 4. to 6. Therefore, it is not possible to evaluate if the inoculum density at the start of the study was within an acceptable range. For study 3., your report that the initial inoculum density was "*5.2 x 10-7 colony forming units / mL*" which is three orders of magnitudes higher than the specifications of OECD TG 301B.

Reporting of the methodology

- For a study according to OECD TG 301B and 301D, the calculation of the $ThCO_2$ and ThOD, respectively, is described and justified;

  However, this information is not provided for studies 1., 2., 4. and 6.

Due to these significant deficiencies, the sources of information 1. to 6. do not provide an adequate and reliable coverage of the key parameter addressed in OECD TG 301B or 301D. Therefore, the reliability of such information in support of your weight of evidence adaptation under Annex XI, Section 1.2 is considered low.

Conclusion on your weight of evidence adaptation:

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

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in a ready biodegradability study according to OECD TG 301 or 310. Therefore, your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision, you explain that you intend to adapt this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across approach') using information on the similar substance Reaction mass of 4-hydroxybenzene-1,3-disulphonic acid and 4-hydroxybenzenesulphonic acid and sulphuric acid and water (EC number 938-815-7). You specify that the study on the similar substance will be generated in the context of an ongoing compliance check for that substance. You have provided a brief description of the proposed read-across approach including compositional information on the target and source substance, some basic physico-chemical properties and the outcome from structural alert profilers form the QSAR Toolbox v.4.4.

In the absence of a comprehensive read-across justification document and of the results of the study on the analogue substance, ECHA is not in a position to make an assessment of the validity of the proposed adaptation.

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

1. In vitro cytogenicity study in mammalian cells or in vitro micronucleus study

An *in vitro* cytogenicity study in mammalian cells or an in vitro micronucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

You have adapted this information requirement under Annex XI, Section 1.5 (read-across). In support of your adaptation, you have provided the following information:

1. an *in vitro* mammalian Chromosome Aberration test (OECD TG 473) on p-toluene sulfonic acid (EC number 203-180-0) in Chinese hamster lung fibroblasts (V79) ([redacted], 1988).
2. an *in vitro* mammalian Chromosome Aberration test (OECD TG 473) on sodium p-toluene sulfonate (EC number 235-088-1) in Chinese hamster lung (CHL/IU) cells ([redacted], 2001).

We have assessed this information and identified the following issues:

A. Rejected read-across adaptations

As explained under Section 1 of the appendix on 'Reasons common to several requests', your read-across adaptations under Annex XI, Section 1.5. for the 'Aromatic sulphonic acids and salts' category is rejected.

B. The studies 1. and 2. are also not in line with the requirements in OECD TG 473

To fulfil the information requirement, the study has to be an *in vitro* chromosomal aberration test or an *in vitro* micronucleus test, conducted in mammalian cells in accordance with OECD TG 473 or OECD TG 487, respectively[3]. The key specifications of these test guidelines include:

a) at least 300 well-spread metaphases must be scored per concentration;
b) the response for the concurrent negative control must be inside the historical control range of the laboratory;
c) data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures must be reported.

The reported data for the studies did not include:

a) the scoring of at least 300 metaphases per concentration is not reported in study 1. In study 2., only 200 metaphases were scored per concentration;
b) reporting on whether the negative control's response is inside the historical control range of the laboratory.
c) reporting on the cytotoxicity and/or the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures.

Therefore, none of the studies listed above meets the information requirement.

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision, you explain that you intend to adapt this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across approach') using information on the similar substance Reaction mass of 4-hydroxybenzene-1,3-disulphonic acid and 4-hydroxybenzenesulphonic acid and sulphuric acid and water (EC number 938-815-7). You specify that the study on the similar substance will be generated in

[3] ECHA Guidance R.7a, Table R.7.7-2, p.557

the context of an ongoing compliance check for that substance. You have provided a brief description of the proposed read-across approach including compositional information on the target and source substance, some basic physico-chemical properties and the outcome from structural alert profilers form the QSAR Toolbox v.4.4.

In the absence of a comprehensive read-across justification document and of the results of the study on the analogue substance, ECHA is not in a position to make an assessment of the validity of the proposed adaptation.
On this basis, the information requirement is not fulfilled.

2. 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.

i. Triggering of the study

Your dossier contains read-across adaptations for *in vitro* gene mutation study in bacteria, and *in vitro* cytogenicity study in mammalian cells or in vitro micronucleus study.

However, the information for the *in vitro* gene mutation study in bacteria and for the *in vitro* cytogenicity study in mammalian cells (or *in vitro* micronucleus study) provided in the dossier are rejected for the reasons provided in appendices A.1. and B.1. above.

The result of the requests for information in appendices A.1. and B.1. above 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.

ii. Assessment of information provided

You have adapted this information requirement under Annex XI, Section 1.5 (read-across). In support of your adaptation, you have provided the following information:

1. an *in vitro* DNA damage and/or repair study in *Saccharomyces cerevisiae* on disodium sulphate (EC number 231-800-9) (Siebert *et al.*, 1970);
2. three *in vivo* micronucleus cytogenicity studies on sodium cumene sulphonate (EC number 248-983-7; Fedtke, 1991), on disodium sulphate (EC number 231-820-9; Gocke *et al.*, 1981) and on calcium xylene sulphonate (EC number 248-829-9; [redacted] 1994);
3. an *in vivo* gene mutation study in *Drosophila melanogaster* on disodium sulphate (EC number 231-820-9; Gocke *et al.*, 1981).

We have assessed this information and identified the following issues:

A. Rejected read-across adaptations

As explained under Section 1 and 2 of the appendix on 'Reasons common to several requests', your read-across adaptations under Annex XI, Section 1.5. for the analogue approach with disodium sulphate and the category approach for 'Aromatic sulphonic acids and salts' are rejected.

B. OECD study/ies other than in vitro gene mutation study in mammalian cells

To fulfil the information requirement, a study must be an *in vitro* gene mutation study in mammalian cells and comply with the OECD TG 476 or 490 (Article 13(3) of REACH and ECHA

Guidance R.7, Table R.7.7-2).

Study 1. is not an *in vitro* gene mutation study in mammalian cells, but in fungus. Therefore, the information provided does not cover the key parameters required by the OECD TG 476 or 490.

C. in vivo mammalian gene mutation test is not reliable (or the data is not adequate)

For the data from an *in vivo* mammalian gene mutation study to be considered adequate, the study has to meet the requirements of OECD TG 488, and the specifications of this test guideline include:

a) the study must be performed in rodent tissue cells, and each group must have a minimum of 5 analysable animals (the test can be performed in either sex);
b) data on the mutation frequency for each tissue and for the treated and control groups must be reported.

The reported data for the studies do not include:

a) a study in mammalian cells including 5 animal per group (study 3.);
b) a study performed according to OECD TG 488 (studies 2.) which reported data on the mutation frequency for each tissue and for the treated and control groups.

Therefore, studies 2. and 3. listed above do not cover specifications required by OECD TG 488.

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision, you explain that you intend to adapt this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across approach'). You intend to support this adaptation using information on Source substance(s) that will be tested (or are already tested) with the OECD TG 476 or OECD TG 490. You consider that if similar effects are observed for between the source substances and the target substance in *in vitro* gene mutation in bacteria and *in vitro* chromosome aberration in mammalian cells, this will support a similar mutagenicity potential on gene mutation in mammalian cells. On this basis, you specify that bridging information will be available to support the read-across to the Substance. You intend to provide this information through a dossier update after the final decision has been issued.

In the absence of a comprehensive read-across justification document and of the results of the study on the analogue substance, ECHA is not in a position to make an assessment of the validity of the proposed adaptation.

On this basis, the information requirement is not fulfilled.

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 an information requirement under Annex VIII to REACH (Section 8.7.1.), 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 adapted this information requirement under Annex XI, Section 1.5 (read-across). In support of your adaptation, you have provided the following information:

1. a statement for the endpoints on reproductive toxicity: "*Studies from the hydrotropes*

category are reported as read across for this endpoint. Hydrotropes are the salt form of the sulphonic acids. The 90-day oral rat and oral mouse studies and the 2-year chronic dermal rat and mouse studies included examination of sex organs of both sexes. No treatment related effects were observed on reproductive organs";

2. a supporting screening study for reproductive/developmental toxicity (OECD TG 421) on sodium toluene sulphonate (EC number 235-088-1) by oral administration in rats (MHLW, 2007);
3. a non-guideline one-generation reproductive toxicity test in pig (key study) on disodium sulphate (EC number 231-820-9) ([redacted] 1974).

We have assessed this information and identified the following issues:

A. Rejected read-across adaptations

As explained under the appendix on 'Reasons common to several requests', your read-across adaptations under Annex XI, Section 1.5. are rejected as you have not established that relevant properties of the Substance can be predicted using either data on the analogue disodium sulphate or data on the members of the 'Aromatic sulphonic acids and salts' category.

B. Studies 2. and 3. are not a reliable screening study for reproductive/developmental toxicity

To be considered compliant and to generate information concerning the effects of the Substance on male and female reproductive performance, the study has to meet the requirements of EU B.63/OECD TG 421. The specifications of this test guideline include among others:

a) highest dose level should aim to induce toxic effects in rodents;
b) dosing of the Substance for a minimum of four weeks for males and approx. 63 days for females to cover premating, conception, pregnancy and at least 13 days of lactation;
c) examination of key parameters for toxicity such as body weight, food consumption or thyroid hormone assessment (P0 and F1);
d) examination of offspring parameters such as number and sex of pups, stillbirths and live births, pup body weight/litter weight, anogenital distance, number of nipples/areolae in male pups.

However, in study 2.:

a) the highest dose level did not induce any toxicity and you have not shown that the aim was to induce toxicity. Therefore, the dose level selection was too low, and the study does not fulfil the criterion set in EU B.63/OECD TG 421 or EU B.64/OECD TG 422;
b) the female animals were exposed for 40-44 days. Therefore, the study does not have the required exposure duration, because the exposure does not cover two weeks of premating, pregnancy, and at least 13 days of lactation;
c) body weight, food consumption or thyroid hormone assessment (P0 and F1) have not been performed;
d) number and sex of pups, stillbirths and live births, pup body weight/litter weight, anogenital distance or number of nipples/areolae in male pups have not been reported.

Furthermore study 3. was not performed in a rodent species, and you did not report the exposure duration or any of the key parameters mentioned above.

Therefore, studies 2. and 3. listed above do not cover specifications required by OECD TG 421.

C. If a prenatal developmental study or an EOGRTS is already available

According to Annex VIII, Section 8.7., Column 2, first paragraph, fourth indent, the study does not need to be conducted if a pre-natal developmental toxicity study (OECD TG 414) or an extended one-generation reproductive toxicity study (OECD TG 443) or a two-generation study (OECD TG 416) is already available.

Your statement does not specify details of the studies you refer to as being available or why an EU B.63/OECD TG 421 or EU B.64/OECD TG 422 study does not need to be conducted. In addition, as explained in Section C.2. below, the PNDT study you submitted does not comply with the respective information requirement. Finally, the exposure duration of a PNDT study does not cover the period from implantation to the late days of pregnancy.

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision, you stated that the study does not need to be conducted if a pre-natal developmental toxicity study (OECD TG 414) is available. Since there is no compliant OECD TG 414, (and no OECD TG 443 nor 416) study available you explained that you will consider other OECD TG 414 data on analgoue substances.

ECHA considers that, in the absence of an adequate pre-natal developmental toxicity study, your justification to omit this information requirement is rejected.

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 an adaptation under Annex XI, Section 1.2. (weight of evidence). In support of your adaptation you have provided the following sources of information:

1. a short-term toxicity study on fish similar to OECD TG 203 with p-toluene sulphonic acid (EC number 203-180-0) ([redacted], 1981);
2. a non-guideline short-term toxicity study on fish with disodium sulphate (EC number 231-820-9) (Trama Francesco, 1954);
3. a short-term toxicity study on fish according to EPA/600/4-90/ 027 with disodium sulphate (EC number 231-820-9) (Mount *et al.*, 1997).

We have assessed this information and identified the following issue:

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.

To fulfil the information requirement on short-term toxicity study on fish, normally a study performed according to OECD TG 203 must be provided. OECD TG 203 investigates the following:

- the concentration of the test material leading to the mortality of 50% of the juvenile fish at the end of the test.

The sources of information 1. to 3. provide relevant information on mortality of the juvenile fish.

However, the reliability of these sources of information is significantly affected by the following deficiencies:

A. The identity of the test material in studies 1. is unclear

For study 1. above, you report that the purity of the test material was [redacted] You have not provided further information, including composition and presence of impurities.

In the absence of composition information, the identity, composition and presence of impurities of the test material cannot be assessed. Therefore, the information provided is rejected.

B. The source of information 1. has low reliability:

To inform on short-term toxicity on aquatic fish, a study must provide equivalent information to study described in the OECD TG 203 test method. Therefore, the following specifications are normally expected to be met:

Validity criteria and characterisation of exposure
- the analytical measurement of test concentrations is conducted;
- in static tests, if the concentrations of the test material are expected to remain within ± 20 % of the nominal, then the test substance concentration is determined (in one replicate) in the highest and lowest test concentrations, and a concentration around the expected LC50 at the beginning and end of the test.

Your registration dossier provides study similar to OECD TG 203 (study 1 above). The test was conducted under static conditions. No analytical verification of exposure was conducted. In the absence of this information, you have not demonstrated that exposure was satisfactorily maintained over the duration of the test and that effect concentrations can be reliably expressed based on nominal concentrations.

Due to these significant deficiencies, the source of information 1. does not provide an adequate and reliable coverage of the key parameter addressed in OECD TG 203. Therefore, the reliability of such information in support of your weight of evidence adaptation under Annex XI, Section 1.2 is considered low.

C. Rejected read-across adaptations

The sub-sections 1 and 2 of the appendix on 'Reasons common to several requests' detail deficiencies with your category approach for 'Aromatic sulphonic acids and salts' and your analogue approach for disodium sulphate (EC 231-820-9). As explained under section 3 of the appendix on 'Reasons common to several requests', these findings apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptations.

In addition to the deficiencies referred to above, we note that you have not provided any reasoning for the prediction of short-term toxicity on fish using the category approach for 'Aromatic sulphonic acids and salts'. However, you consider that:
- *"an environmental risk assessment has indicated that the members of the Aromatic Sulphonic Salt category do not pose a risk to the aquatic environment for all relevant uses"*;
- *"the disulphonated component is expected not to have an impact* [...]".

ECHA understands that you predict the properties of the Substance using a category 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:

- p-toluene sulphonic acid (EC number 203-180-0)

Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances".* ECHA Guidance R.6.2.1.5 clarifies that one of the factors in determining the robustness of a category is the density and distribution of the available data across the category. To identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the category members must be available.

As you have only provided information from a single category member, this information is not sufficient to conclude that short-term toxicity on fish is likely to be similar within the category.

On the basis of the above, you have not established that relevant properties of the Substance can be predicted using either data on the analogue disodium sulphate or data on the members of the 'Aromatic sulphonic acids and salts' category. Therefore, the reliability of such information in support of your weight of evidence adaptation under Annex XI, Section 1.2 is considered low.

Conclusion on your weight of evidence adaptation:

Taken together, even if these sources of information provide information on short-term toxicity on fish, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 203. Therefore, your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision, you explain that you intend to adapt this information requirement under Annex XI, Section 1.5. ('Grouping of substances and read-across approach') using information on the similar substance Reaction mass of 4-hydroxybenzene-1,3-disulphonic acid and 4-hydroxybenzenesulphonic acid and sulphuric acid and water (EC number 938-815-7). You specify that the study on the similar substance will be generated in the context of an ongoing compliance check for that substance. You have provided a brief description of the proposed read-across approach including compositional information on the target and source substance, some basic physico-chemical properties and the outcome from structural alert profilers form the QSAR Toolbox v.4.4.

In the absence of a comprehensive read-across justification document and of the results of the study on the analogue substance, ECHA is not in a position to make an assessment of the validity of the proposed adaptation.

5. Adsorption/ desorption screening

Adsorption/desorption screening is an information requirement under Annex VIII to REACH (Section 9.3.1.).

You have provided the following information:

1. an adaptation under Section 9.3.1., column 2 of Annex VIII with the following justification:
   - *"the substance has a very low log Pow and therefore is likely to have a very low potential for absorption";*
   - *"the substance is readily biodegradable".*

We have assessed this information and identified the following issues:

A. Under Section 9.3.1., column 2 of Annex VIII, the study may be omitted if based on the physicochemical properties the substance can be expected to have a low potential for adsorption (e.g. the substance has a low octanol water partition coefficient). To adapt this information requirement based on low Log Kow only, lipophilicity must be the sole characteristic driving the adsorption potential of a substance. However, for some groups of substances (e.g. ionisable substances, surfactants) other mechanisms than lipophilicity may drive adsorption.

   You have justified the low potential for adsorption because the partition coefficient value (log Kow) was predicted to be -4.43 (based on KOWWIN v 1.68). You consider that the Substance is fully dissociated in water.

   While anionic substances may be expected to have lower tendency to sorb compared to cationic substances, ionic binding to positively charged soil constituents (e.g. hydrous oxides of aluminium and iron) cannot be excluded. Therefore, log Kow is not a valid descriptor for assessing the adsorption potential of the Substance and your adaptation is rejected.

B. Under, Section 9.3.1., column 2 of Annex VIII, the study may be omitted if the substance is readily biodegradable.

   For the reasons explained under Section A.4., the information requirement on ready biodegradability is not fulfilled. Therefore, you have not demonstrated that the substance is readily biodegradable, and your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

We take note of your intention explained in the comments on the draft decision, to adapt this information requirement under Section 9.3.1., column 2 of Annex VIII if the results of the ready biodegradability on the similar substance Reaction mass of 4-hydroxybenzene-1,3-disulphonic acid and 4-hydroxybenzenesulphonic acid and sulphuric acid and water (EC number 938-815-7) shows it is readily biodegradable.

ECHA takes note of your intention. However, in the absence of an appropriate read-across justification, ECHA is not in a position to assess the validity of such approach.

Appendix C: Reasons to request information required under Annex IX of REACH

1. Sub-chronic toxicity study (90-day) Sub-chronic toxicity study (90-day)

A Sub-chronic toxicity study (90 day) is a standard information requirement in Annex IX to REACH.

You have adapted this standard information requirement under Annex XI, Section 1.2. (weight of evidence). In support of your adaptation, you have the following information:

1. A sub-chronic (90-day) toxicity study in rats performed with sodium xylene sulphonate (EC number 215-090-9) (OECD TG 408, reliability 2; [redacted], 1969);
2. a dose-range finding study (14-day repeated dose) in mice with sodium xylene sulphonate (EC number 215-090-9) (reliability 2, 1979);
3. a sub-chronic (90-day) oral test in male and female mice performed with sodium xylene sulphonate (EC number 215-090-9) (reliability 2, 1980);
4. a dose-range finding study (14-day repeated dose) in rats performed with sodium xylene sulphonate (EC number 215-090-9) (reliability 2, 1980);
5. a chronic oral study (Enhancement of Azo fe Carcinogenesis) in rats performed with disodium sulphate (EC number 231-820-9) (reliability 2; Blunck and Crowther, 1975);
6. a 4-week repeated dose oral study in rats with disodium sulphate (EC number 231-820-9) (reliability 2; [redacted], 1960);
7. a 28-day study in pigs, given water with added sulphate from disodium sulphate (EC number 231-820-9) (supporting study; reliability 2; Paterson, 1979);
8. a 90-day experiment in Angus heifers, given inorganic sulphate in drinking water (EC number 231-820-9) (supporting study, reliability 2; Digesti *et al.*, 1976);
9. a 28-day repeated dose oral study in rats performed with sodium toluene sulphonate (EC number 235-008-1) (OECD TG 407, reliability 2; [redacted], 2001).

To justify your weight of evidence approach, you have stated that "*the key study is a 90-day oral study, conducted in 1968, [as it] is generally comparable to the OECD 408 guideline study. [...]*" and you have justified your selection: "*Despite [being] the oldest one, the 1969 study is the most similar to OECD 408 guideline. Result and details are well described. The study is performed on an analogous sulphonated of the substance component hydroxybenzene disulphonated [...] being more hydrophilic and excreted more quickly is expected to express a lower level of toxicity, as in many literature studies where the sulphonation degree is a key factor in diminishing the toxicity. [...] Therefore the result for this substance can be taken into account as a conservative value for risk assessment.*"

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.

To fulfil the information requirement on sub-chronic (90-day) repeated dose toxicity, normally a study performed according to OECD TG 408 must be provided. OECD TG 408 requires to investigate the following:

- detection and quantification of adverse effects in various target organs, following oral administration for a period of 90 days and subsequent systemic availability of the Substance;
- detection and reporting of variations and malformations in organs and tissues, including thyroid, sexual organs.

Because they are performed for a shorter duration (namely 14 or 28 days), the studies 2., 4.,

6., 7. and 9. are not relevant for this endpoint. Consequently, only the sources of information 1, 3., 5. and 8. provide relevant information on the findings following repeated oral administration for a period of 90 days and detection and reporting of effects exerted as a result of such a repeated administration.

However, the reliability of these sources of information is significantly affected by the following:

A. *The sources of information 1., 3., 5. and 8. have low reliability:*

To inform on sub-chronic (90 days) repeated dose toxicity, a study must provide equivalent information to study described in the OECD TG 408 test method. Therefore, the following specifications are normally expected to be met:

a) at least three dose levels and a concurrent control are tested;
b) the highest dose level must aim to induce some systemic toxicity, but not death or severe suffering;
c) at least 10 female and 10 male rodents are used at each dose level (including control group);
d) clinical observations, ophthalmological examination, sensory reactivity to various stimuli and functional observations of the animals, recording of body weight, haematology, clinical biochemistry, and pathology of sexual (male and female) organs, full detailed gross necropsy and subsequent histopathology of both types tissues are included.

However,

a) the studies 5. and 8. were conducted with less than three dose levels;
b) the highest dose level in the studies 3. and 5. did not induce any systemic toxicity in females. Therefore, the dose level selection was too low;
c) the study 5. was conducted with less than 10 animals per sex per test dose group. The statistical power of the information provided is not sufficient because it does not fulfil the criterion of 20 animals (10 males + 10 females) for each test group. In addition, the study 8. was performed in a different species than rodent;
d) The study 1. did not include information on clinical, ophthalmological and neurobehavioral observations. The studies 2. and 3. did not include functional observations or ophthalmoscopy. Study 3. also lacks information on clinical chemistry and on haematology.

B. *Rejected read-across adaptations*

The sections 1 and 2 of the appendix on 'Reasons common to several requests' detail deficiencies with your category approach for 'Aromatic sulphonic acids and salts' and your analogue approach for disodium sulphate (EC number 231-820-9). As explained under section 3 of the appendix on 'Reasons common to several requests', these findings apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptation.

On the basis of the above, you have not established that relevant properties of the Substance can be predicted using either data on the analogue disodium sulphate or data on the members of the 'Aromatic sulphonic acids and salts' category. Therefore, the reliability of such information in support of your weight of evidence adaptation under Annex XI, Section 1.2 is considered low.

Conclusion on your weight of evidence adaptation:

Taken separately the sources of information do not provide reliable information with regards to the OECD TG 408 specifications. Taken together, even if they provide some information on sub-chronic repeated dose toxicity, the reliability of these sources is affected by the rejection of your category and read-across approaches, so significantly that they cannot be taken into consideration in a weight of evidence approach.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 408. Therefore, your adaptation is rejected.

In your comments on the draft decision, you agreed that the source studies you provided in your registration dossier are not adequate to fulfil the information requirement. However, you disagreed to conduct a study on the Substance. ECHA takes note of your intention to rather rely on studies on the individual components of the multi-constituent substance, and to adapt your read-across hypothesis and your read-across adaptations.

However, based on the above and on the information currently available, the information requirement is not fulfilled.

Study design

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, when the Substance is a highly soluble solid substance. Therefore, the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance.

2. Pre-natal developmental toxicity study in one species

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

You have adapted this information requirement under Annex XI, Section 1.5 (read-across). In support of your adaptation, you have provided the following information:

1. A developmental Toxicity (key) Study in Rats (no test guideline, 1994) performed with calcium xylene sulphonate (EC number 248-829-9);
2. A non-guideline (key) study (to assess teratogenic effects of various sulphated substances) performed with disodium sulphate (EC number 231-820-9) as anion control (reliability 2; Arcuri & Gautieri, 1973);
3. A preliminary oral screening test performed with sodium toluene sulphonate (EC number 235-088-1) (OECD TG 421, reliability 2; MHLW, 2007).

We have assessed this information and identified the following issues:

A. Rejected read-across adaptations

As explained under the appendix on 'Reasons common to several requests', your read-across adaptations under Annex XI, Section 1.5. are rejected as you have not established that relevant properties of the Substance can be predicted using either data on the analogue disodium sulphate or data on the members of the 'Aromatic sulphonic acids and salts' category.

B. The studies provided are not reliable pre-natal developmental toxicity studies

The study 3. does not provide information following OECD TG 414 as it does not inform on skeletal and visceral malformations and variations as required by OECD TG 414. Also, the animal numbers examined are lower compared to the specifications of OECD TG 414.

To fulfil the information requirement, a study must comply with the OECD TG 414. The criteria of this test guideline include:

a) highest dose level should aim to induce some developmental and/or maternal toxicity;
b) examination of the dams for weight and histopathology of the thyroid gland/thyroid hormone measurements/gravid uterus weight/uterine content/body weight of the dams/clinical signs of the dams;
c) examination of the foetuses for sex and body weight/external, skeletal and soft tissue alterations (variations and malformations)/number of resorptions and or live foetuses/ measurement of anogenital distance in live rodent foetuses.

However,

a) in study 1., the highest dose level did not induce any developmental and/or maternal toxicity and you have not shown that the aim was to induce toxicity. Therefore, the dose level selection was too low;
b) in either studies 1. or 2., you have not reported whether the weight and histopathology of the thyroid gland, the thyroid hormone measurements have been conducted in dams, or whether the gravid uterus weight have been examined or measured as required in OECD TG 414;
c) you have not reported whether the sex and body weight of the foetuses, external, skeletal and soft tissue alterations (variations and malformations) have been examined as required in OECD TG 414.

In your comments on the draft decision, you agreed that the study you provided in your registration dossier is not in line with the requirements of OECD TG 414. ECHA takes note of your intention to rather rely on studies on the individual components of the multi-constituent substance, and to adapt your read-across hypothesis and your read-across adaptations.

However, based on the above and on the information currently available, the information requirement is not fulfilled.

Study design

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[4] administration of the Substance.

3. Long-term toxicity testing on aquatic invertebrates

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

You have provided an adaptation under Section 9.1.5., column 2 of Annex IX. In support of your adaption you provided the following justification:

- "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".
- *"an environmental risk assessment has indicated that the members of the Aromatic Sulphonic Salts category do not pose a risk to the aquatic environment for all relevant uses"*;
- *"Sodium sulphate has a low potential for bioaccumulation and aquatic toxicity is*

[4] ECHA Guidance R.7a, Section R.7.6.2.3.2.

unlikely to occur".

You also provided an adaptation under Annex XI, Section 1.2. (weight of evidence) supported by the following sources of information:

1. an extract from the Database U.S. EPA ECOTOX, Version 4 with disodium sulphate (EC number 231-820-9) (2013);
2. a non-guideline long-term toxicity test to aquatic invertebrates with disodium sulphate (EC number 231-820-9) (Soucek, 2007);

We have assessed this information and identified the following issues:

A. Annex IX, Section 9.1, Column 2

Annex IX, Section 9.1, Column 2 is not a waiver for the requirement to submit information on long-term toxicity to fish under Column 1 but a trigger for providing further information on long-term toxicity to fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018). Therefore, your claimed adaptation is rejected.

B. Your weight of evidence adaptation

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.

To fulfil the information requirement on long-term toxicity study on aquatic invertebrates, normally a study performed according to OECD TG 211 must be provided. OECD TG 211 investigates the following:

1) the reproductive output of *Daphnia* sp. expressed as the total number of living offspring produced at the end of the test, and
2) the survival of the parent animals during the test, and
3) the time to production of the first brood.

The sources of information 1. and 2. provide relevant information on long-term toxicity on aquatic invertebrates.

However, the reliability of these sources of information is significantly affected by the following deficiencies:

The sub-sections 1 of the appendix on 'Reasons common to several requests' details deficiencies with your analogue approach for disodium sulphate (EC 231-820-9). As explained under section 3 of the appendix on 'Reasons common to several requests', these findings apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptations.

On the basis of the above, you have not established that relevant properties of the Substance can be predicted using data on the analogue disodium sulphate. Therefore, the reliability of such information in support of your weight of evidence adaptation under Annex XI, Section 1.2 is considered low.

Conclusion on your weight of evidence adaptation:

Taken together, even if these sources of information provide information on long-term toxicity on aquatic invertebrates, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 211. Therefore, your adaptation is rejected.

In your comments on the draft decision, you claim that you did not perform a long-term toxicity testing on aquatic invertebrates because the chemical safety assessment according to Annex I does not indicate the need to investigate further the effects on aquatic organisms. You also specify that new information on short-term aquatic toxicity will be provided and that it will be used to update your chemical safety assessment. You argue that depending on the outcome of the chemical safety assessment you will decide if long-term aquatic toxicity tesing is needed. You also specify that you intend to test only the most sensitive aquatic organism among fish and aquatic invertebrates.

However, as already explained under issue A. above, Annex IX, Section 9.1, Column 2 is not a waiver for the requirement to submit information on long-term toxicity to fish. Therefore any adaptation to omit this information requirement will need to rely on the general rules for adaptation set out in Annex XI to REACH.

On this basis, the information requirement is not fulfilled.

4. Long-term toxicity testing on fish

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

You have provided an adaptation under Section 9.1.6., column 2 of Annex IX. In support of your adaption you provided the following justification:

- *"an environmental risk assessment has indicated that the members of the Aromatic Sulphonic Salts category do not pose a risk to the aquatic environment for all relevant uses"*;
- *"Sodium sulphate has a low potential for bioaccumulation and aquatic toxicity is unlikely to occur"*.

We have assessed this information and identified the following issue:

Annex IX, Section 9.1, Column 2 is not a waiver for the requirement to submit information on long-term toxicity to fish under Column 1 but a trigger for providing further information on long-term toxicity to fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018). Therefore, your claimed adaptation is rejected.

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision, you claim that you did not perform a long-term toxicity testing on fish because the chemical safety assessment according to Annex I does not indicate the need to investigate further the effects on aquatic organisms. You also specify that new information on short-term aquatic toxicity will be provided and that it will be used to update your chemical safety assessment. You argue that depending on the outcome of the chemical safety assessment you will decide if long-term aquatic toxicity tesing is needed. You

also specify that you intend to test only the most sensitive aquatic organism among fish and aquatic invertebrates.

However, as already explained under issue A. above, Annex IX, Section 9.1, Column 2 is not a waiver for the requirement to submit information on long-term toxicity to fish. Therefore any adaptation to omit this information requirement will need to rely on the general rules for adaptation set out in Annex XI to REACH.

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

Appendix D: 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[5].

B. Test material

1. Selection of the Test material(s)

   The Test Material used to generate the new data must be selected taking into account the following:
   - the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

2. Information on the Test Material needed in the updated dossier
   - You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   - The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

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

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[6].

[5] https://echa.europa.eu/practical-guides
[6] https://echa.europa.eu/manuals

Appendix E: 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 F: 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 13 February 2020.

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

ECHA took into account your comments and did not amend the requests.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix G: List of references - ECHA Guidance[7] 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)[8]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[8]

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[9]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

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

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

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

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

Appendix H: 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.