~~Confidential~~

Helsinki, 06 September 2021

Addressees
Registrant(s) of JS PHENOLSULPHONATED UVCB as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
28/03/2018

Registered substance subject to this decision ("the Substance")
Substance name: Phenol, sulfonated
EC number: 277-962-5
CAS number: 74665-14-8

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 ***12 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) on relevant constituent(s) of the Substance or on the whole Substance

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. If negative results are obtained in test performed for the information requirement of Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

3. Short-term repeated dose toxicity (28 days) (Annex VIII, Section 8.6.1.; test method: EU B.7./OECD 407) by oral route, in rats

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

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

- Appendix entitled "Reasons common to several requests";
- Appendix/Appendices entitled "Reasons to request information required under Annexes VII to VIII of REACH", respectively.

Information required depends on your tonnage band

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

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

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

How to comply with your information requirements

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

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

Appeal

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

Failure to comply

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

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

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

Appendix on Reasons common to several requests

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

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

- 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.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

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

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

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

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

You have not included a justification for your weight of evidence adaptation, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Irrespective of the above mentioned deficiencies on the documentation, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided sources of information.

ECHA has assessed the validity of your adaptation and identified the following issues:

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

1.1. Reliability of the provided information with analogue substances

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

Grouping of substances and read-across approach

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

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

You have provided a read-across justification document in IUCLID Section 13, entitled [redacted] hereafter "justification document".

In the justification document you state that *"The chemical intermediate phenol, sulfonated EC277-962-5, CAS74665-14-8 is a complex mixture of molecules mainly composed of [redacted] (see section 1.2 of the dossier for the detailed composition).*

You propose to predict the properties of your Substance using data from "[…] *similar substances of the constituents of Phenol, sulfonated*", as listed below:

1. Hydroxybenzenesulphonic acid (EC: 215-587-0; CAS: 1333-39-7)
2. Benzenesulphonic acid, dimethyl- (EC: 246-839-8; CAS 25321-41-9)
3. Benzenesulphonic acid (EC: 202-638-7; CAS: 98-11-3)
4. p-Toluenesulphonic acid (EC: 203-180-0; CAS: 104-15-4)
5. Sodium cumenesulfonate EC: 248-983-7; CAS: 28348-53-0)
6. Calcium bis[(4-methylphenyl)methanesulfonate (EC: 248-829-9; CAS: 28088-63-3)
7. Xylenesulfonic acid, sodium salt (EC: 215-090-9; CAS: 1300-72-7)
8. Xylenesulfonic acid, ammonium salt (EC: 247-710-9; CAS 26447-10-9)

You conclude that *"The chemical structures of the similar substances are comparable to the chemical structure of the constituents of Phenol, sulfonated (UVCB)".*

You state that *"A category approach based on the main components aromatic sulphonic acids can be taken into account for the hazard evaluation of the whole UVCB substance"* and that "*The studies with the salts (hydrotropes) provide valid read-across for the acids […] therefore the dataset for the entire hydrotropes category can be applied broadly".*

On the basis of this information ECHA understands that you have applied a constituent-based approach whereby you conclude on the properties of the Substance using the results obtained from independent studies conducted with source substances, structurally similar to the

[2] ECHA Guidance R.6

constituents of your UVCB Substance.

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. Thus, the (eco)toxicological properties of the Substance are predicted to be quantitatively equal to those of the source substances.

ECHA has analysed your approach and has identified the following issues:

1. Missing information on the link between the source substances and the constituents of the Substance

As indicated above, your hypothesis is based on the assumption that the source substances which you consider structurally similar to the constituents of your Substance can be used to predict the properties of these constituents and when taken together, to determine the (eco)toxicological properties of the Substance. In this context, you must explain how you intend to assess the properties of the whole Substance and why properties of the whole Substance can be derived from information on the selected source substances.

The Substance is a complex mixture of [redacted], some of which are isomers.
In your justification document you have provided a list of "similar substances" (thereafter referred to as 'source substances') that you consider structurally similar to the constituents of the Substance.

ECHA notes that there are major structural differences between the constituents of the Substance and the source substances. In particular, the source substances contain functional groups attached to the phenyl ring (e.g. [redacted]) that are not present in the structure of the constituents of your Substance. You did not explain which source substance(s) would inform on the properties of which constituent(s) of the Substance. You also did not explain how you consider that the information from these source substances can reliably contribute to the identification of the properties of the Substance despite the identified structural differences between these substances.
Therefore, you have not clearly and unambigously established the basis of your constituent-based read-across approach.

2. Lack of documentation regarding the provided information with source substance sodium 4-methylbenzenesulfonate (EC: 211-522-5, CAS: 657-84-1)

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).[3]

ECHA notes that the source substance sodium 4-methylbenzenesulfonate (EC: 211-522-5, CAS: 657-84-1) is not referred to in your read-across justification document, but source studies performed with this source substance are included in the technical dossier for the following ecotoxicological information requirements:

- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

[3] ECHA Guidance R.6, Section R.6.2.6.1

ECHA understands that you have provided studies conducted with sodium 4-methylbenzenesulfonate in order to comply with the above listed REACH information requirements. You have not provided documentation, containing the necessary elements as described above, 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.

Conclusion for prediction of (eco)toxicological properties

Based on the above, the information from the source substances submitted under your weight of evidence adaptation is not considered reliable. As indicated further above, additional issues related to your weight of evidence adaptations are addressed under the corresponding information requirement(s).

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 a standard information requirement under Annex VII to the REACH Regulation (Section 8.4.1.).

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH (weight of evidence).

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

(i) *In vitro* gene mutation study in bacteria (no guideline soecified, no GLP), performed with benzenesulphonic acid (EC: 202-638-7; CAS: 98-11-3), giving negative results.
(ii) *In vitro* gene mutation study in bacteria (equivalent to OECD TG 471, GLP), performed with p-toluenesulphonic acid (EC: 203-180-0 104-15-4; CAS: 104-15-4), giving negative results.

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

Relevant information for this endpoint can be obtained from OECD TG 471.

As pointed out under Section '1.1. Reliability of the provided information with analogue substances' under the Appendix on Reasons common to several requests, you have not established the basis of your constituent-based read-across approach. Therefore, it is not clear how you intend to cover the mutagenicity properties of the Substance by using the sources of information on the selected source substances. Due to this major deficiency ECHA cannot assess the relevance and relability of the sources of information provided as part of this weight of evidence against the information requirement stated in the OECD TG 471.

Conclusion

It is not possible to conclude, whether your Substance has or has not the particular dangerous properties foreseen to be investigated *in vitro* gene mutation study in bacteria. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

In your comments to the draft decision, you agree to perform the requested study.

Information on the study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation test in bacteria using 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) is applicable.

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 adapted this standard information requirement according to Annex XI, Section 1.2. of REACH (weight of evidence).

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

(i) A study according to OECD TG 202 conducted on benzene sulphonic acid (EC: 202-638-7; CAS 98-11-3) [redacted], 1995
(ii) A study according to OECD TG 202 conducted on benzene sulphonic acid (EC: 202-638-7; CAS 98-11-3) [redacted] 2005
(iii) A study according to OECD TG 202 conducted on toluene-4-sulphonic acid, EC 203-180-0, CAS 104-15-4 [redacted], 2010

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

Relevant information for this endpoint can be obtained from OECD TG 202.

As pointed under Section '1.1. Reliability of the provided information with analogue substances' under the Appendix on Reasons common to several requests, you have not established the basis of your constituent-based read-across approach. Therefore, it is not clear how you intend to cover the short-term toxicity on aquatic invertebrates properties of the Substance by using the sources of information on the selected source substances. Due to this major deficiency ECHA cannot assess the relevance and relability of the sources of information provided as part of this weight of evidence against the property investigated by an OECD TG 202 study.

Conclusion

It is not possible to conclude whether your Substance has or has not the particular dangerous properties foreseen to be investigated in a short-term toxicity study on aquatic invertebrates. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

In your comments to the draft decision, you agree to perform the requested study.

Study design
The Substance is difficult to test due to the adsorptive properties (due to the Substance being ionisable, pKa = 3.2). OECD TG 202 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

For multi-constituents/UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the

test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key constituents or groups of constituents).

If you decide to use the Water Accommodated Fraction (WAF) approach, in addition to the above, you must:

- use loading rates that are sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (ECHA Guidance, Appendix R.7.8.1-1, Table R.7.8-3);
- provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any remaining non-dissolved test material including a justification for the separation technique);
- prepare WAFs separately for each dose level (i.e. loading rate) and in a consistent manner.

3. Growth inhibition study aquatic plants

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

You have adapted this standard information requirement according to Annex XI, Section 1.2. of REACH (weight of evidence).

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

(i) A study according to EU method C.3 conducted on sodium 4-methylbenzenesulfonate (EC: 211-522-5; CAS 657-84-1) – [redacted] 1995

(ii) A study according to EPO OTS method conducted on calcium xylenesulphonate (no identifiers provided) - [redacted], 1994

(iii) A study according to EPO OTS method conducted on sodium xylene sulphonate (no identifiers provided) - [redacted] 1993

(iv) A study according to OECD TG 201 conducted on benzenesulphonic acid (EC: 202-638-7; CAS 98-11-3)

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

Relevant information for this endpoint can be obtained from OECD TG 201.

As pointed out under Section '1.1. Reliability of the provided information with analogue substances' under the Appendix on Reasons common to several requests, you have not established the basis of your constituent-based read-across approach. Therefore, it is not clear how you intend to cover the algae growth inhibition properties of the Substance by using the sources of information on the selected source substances. Due to this major deficiency ECHA cannot assess the relevance and relability of the sources of information provided as part of this weight of evidence against the property investigated by an OECD TG 201 study.

Conclusion
It is not possible to conclude whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an algae growth inhibition study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

In your comments to the draft decision, you agree to perform the requested study.

Study design
OECD TG 201 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Section A.2.

4. Ready biodegradability

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

You have adapted this standard information requirement according to Annex XI, Section 1.2. of REACH (weight of evidence).

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

(i) A study according to OECD TG 301B conducted on sodium 2-phenylpropane-2-sulfonate (EC: 248-983-7; CAS: 28348-53-0) - [redacted], Inc, 1993 (Report # [redacted])

(ii) A study according to OECD TG 301B conducted on sodium xylenesulphonate (EC 215-090-9; CAS: 1300-72-7) - [redacted], 1993 (Report # [redacted])

(iii) A publication not mentioning guideline followed conducted on p-toluene sulfonic acid, EC 203-180-0, CAS 104-15-4 - Matsui, Okawa, Ota, 1988

*(iv)*A study according to OECD TG 301D conducted on sodium xylenesulphonate (EC: 215-090-9; CAS: 1300-72-7) - [redacted]. (sponsor), 1995

(v) A publication not mentioning guideline followed conducted on benzene sulfonic acid (EC: 202-638-7; CAS: 98-11-3) - Kawahara, Yakabe, Ohide, Kida 1999

(vi) A publication not mentioning guideline followed conducted on benzene sulfonic acid, (EC: 202-638-7; CAS 98-11-3) - Kawasaki, 1980

(vii) A review article following different guidelines conducted on p-toluene sulfonic acid (EC: 203-180-0; CAS: 104-15-4) - Bayer, 1991

(viii) A study according to EU method C.6 conducted on benzene sulphonic acid (EC: 202-638-7; CAS: 98-11-3) - [redacted], 1976

(ix) A study according to EU method C.6 conducted on p-toluene sulfonic acid (EC: 203-180-0; CAS: 104-15-4) - [redacted] 1976

(x) A study according to OECD TG 301B conducted on sodium 4-methylbenzenesulfonate (EC: 211-522-5; CAS: 657-84-1) - [redacted] 2004

(xi) A study according to OECD TG 301B conducted on sodium xylenesulfonate (EC: 215-090-9; CAS: 1300-72-7) [redacted], 1993

(xii) A study not mentioning guidline followed conducted on benzene sulfonic acid, (EC: 202-638-7; CAS: 98-11-3) - [redacted], 1989

(xiii) A study not mentioning guidline followed conducted on p-Hydroxybenzensulfonic acid (EC: 202-691-6) - [redacted], 1966

(xiv) A study according to OECD TG 301B conducted on calcium xylenesulphonate (EC: 248-829-9; CAS: 28088-63-3) - [redacted], 1994

(xv) A study according to OECD TG 301D conducted on benzene sulfonic acid (EC: 202-638-7; CAS: 98-11-3) - [redacted], 1995

(xvi) A study according to OECD TG 301D conducted on sodium cumenesulphonate (EC: 248-983-7; CAS: 28348-53-0) - [redacted] 1995

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

Relevant information for this endpoint can be obtained from OECD TG 301 or OECD TG 310.

As pointed out under Section '1.1. Reliability of the provided information with analogue substances' under the Appendix on Reasons common to several request, you have not established the basis of your constituent-based read-across approach. Therefore, it is not clear how you intend to cover the ready biodegradability properties of the Substance by using the sources of information on the selected source substances. Due to this major deficiency ECHA cannot assess the relevance and relability of the sources of information provided as part of this weight of evidence against the property investigated by an OECD TG 301 or OECD TG 310 study.

Conclusion
It is not possible to conclude whether your Substance has or has not the particular dangerous properties foreseen to be investigated in a ready biodegradability study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

Considerations on the study design
Reliable information on all relevant constituents (> 0.1% (w/w)) is required for the purpose of PBT/vPvB assessment (ECHA Guidance R.11, Section R.11.4.2.2).

The ready biodegradability tests, such as OECD TG 301 or 310, are intended for pure substances and are generally not applicable for complex compositions containing different types of constituents, like UVCBs. For a UVCB substance with constituents of variable properties, observed biodegradation may represent the biodegradation potential of only some of the constituents (ECHA Guidance R.11, Section R.11.4.2.2).

Revised Introduction to the OECD Guidelines for Testing of Chemicals, Section 3 - Part 1: Principles and strategies related to the testing of degradation of organic chemicals[4] recommends that *"a case by case evaluation should take place on whether a biodegradability test on such a complex mixture would give valuable information regarding the biodegradability of the mixture as such (i.e. regarding the degradability of all the constituents) or whether instead an investigation of the degradability of carefully selected individual components of the mixture is required.*

In your PBT/vPvB assessment, you conclude that the Substance is not P/vP because it is readily biodegradable. You consider that the Substance is readily biodegradable based on sources of information with source substances provided in the dossier and listed above.

[4] http://www.oecd.org/chemicalsafety/testing/34898616.pdf

The Substance is a UVCB and in the composition of the Substance reported in the dossier there is a number of constituents (e.g. [redacted]) that are expected to have different properties, in particular, in terms of solubility, log Kow, bioaccumulation, ecotoxicity and biodegradability. Specifically, biodegradability potential of the constituents of the Substance might be affected, at least, by the number of sulphonated phenols and possible impact of sulphonation (sulfonyl and sulfonyl hydroxide functional groups).

Your conclusion that the Substance is not P/vP based on readily biodegradability is not substantiated due to the following. First, as explained above, there is no reliable and relevant information on ready biodegradability provided in the dossier for the constituents of the Substance. Second, ECHA notes that for one of the constituents of your Substance, i.e. [redacted] with typical concentration of 6.13% (w/w), ECHA's dissemination website contains information showing that [redacted] is not readily biodegradable (0% degradation after 28 days in an OECD TG 301C study)[5]. As a consequence, there is available data on a constituent of the Substance, which you have not included in your dossier, indicating a potential P/vP concern for the Substance.

As your Substance is a complex UVCB containing different types of constituents of variable properties, the ready biodegradability of each constituent of the Substance cannot be determined on the basis of results of studies conducted on the whole Substance.

According to ECHA Guidance R.11 for the purpose of the PBT/vPvB assessment "Known constituents" approach "*can be applied when a substance is 'a priori' known to contain specific constituents at relevant concentrations, these constituents are suspected based on available information to represent the worst case of the (v)P, (v)B and T properties of all constituents of the substance, and these specific constituents can be isolated or separately manufactured or otherwise acquired for the purpose of testing*."

As the Substance is a well characterised UVCB and consists of constituents that are expected to have different properties, ECHA considers that information on ready biodegredability "*of carefully selected individual components"* is relevant for the PBT/vPvB assessment of the Substance. These individual components selected for the testing should be reasonably the most persistent constituent(s) of the Substance. The selection of the most persistent constituent(s) must be justified and reported in the registration dossier. The selection should consider, at least, molecular weight of constituents and the degree of sulfonation of the constituents.

You may start the testing with the worst-case constituent of the Substance.

In your comments to the draft decision, you propose to perform the ready biodegradability test with the whole Substance. As a justification you provide a table with PBT/vPvB information on the constituents of your UVCB Substance.

We have assessed this information and note the following:

As explained above, the OECD "*Guidelines for the Testing of Chemicals, Revised Introduction to the OECD Guidelines for Testing of Chemicals, Section 3 Part I: Principles and Strategies related to the Testing of Degradation of Organic Chemicals*" indicates that ready biodegradability tests are in general intended for pure substances because for UVCB and multiconstituent substances any observed biodegradation may reflect the biodegradation of only some constituents. However, the OECD document indicates also that "*it is sometimes*

[5] https://echa.europa.eu/brief-profile/-/briefprofile/100.001.137

relevant to examine the ready biodegradability of mixtures of structurally similar chemicals", but, as also quoted above, a case by case evaluation should take place on applicability of such information regarding the biodegradability of the mixture or whether instead an investigation of the degradability of carefully selected individual components of the mixture is required.

In your comments to the draft decision, you report the following ready biodegradability information on the constituents (except [redacted] since it is inorganic) of your UVCB Substance :

- None of the organic constituents is readily biodegradable based on QSAR predictions (EpiSuite BIOWIN v4.10).
- One constituent ([redacted]) is not readily biodegradable also based on experimental information provided on ECHA's dissemination website.
- One constituent ([redacted]) is readily biodegradable based on information provided on ECHA's dissemination website.

Based on the reported information you propose to conduct the ready biodegradability test with the whole Substance.

ECHA agrees that no information on ready biodegradability is needed for the inorganic constituent. ECHA notes that the disseminated ready biodegradation data on EC 202-691-6 is not reliable, as assessed in a compliance check for that substance (CCH-D-2114493626-36-01/F)[6].

The other ready biodegradability information provided in your comments indicates that the constituents of the Substance are homogeneous in terms of their biodegradability because all of the results are negative i.e. demonstrate that none of the constituents is ready biodegradable. As a consequence, ECHA considers your proposal to conduct an experimental ready biodegradation study on the whole Substance as also appropriate to address the identified incompliance, as negative result can be expected. However, as already noted above, in case positive result would be obtained this may not be sufficient to consider the UVCB Substance as ready biodegradable. Positive results must be unequivocal (ECHA Guidance R.7b, Section R.7.9.4.1) and for the UVCB substance it would have to be demonstrated by scientific evidence why the results can be used to represent the variety of constituents.

To conclude, taking into account all of the above ECHA amended the request to reflect the provided alternative of testing the whole Substance.

[6] https://echa.europa.eu/documents/10162/5ac8af44-b083-bbf2-52d1-31d73c151177

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 a standard information requirement in Annex VIII to REACH.

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

In support of your adaptation, you have provided the following study records with source substances:

(i) *In vitro* cytogenicity in mammalian cells (OECD TG 473, GLP, KL 2) performed with p-toluenesulphonic acid (EC: 104-15-4; CAS: 203-180-0), giving negative results.

(ii) *In vivo* mammalian erythrocyte micronucleus test (OECD TG 474, GLP), performed with sodium 2-phenylpropane-2-sulfonate EC: 248-983-7; CAS: 28348-53-0).

(iii) *In vivo* bone marrow chromosome aberration (according to EPA OTS 798.5385, GLP), performed with calcium xylenesulphonate (EC: 248-829-9; CAS: 28088-63-3).

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

Relevant information for this endpoint can be obtained from *in vitro/in vivo* chromosomal aberration tests (OECD TG 473/OECD TG 475) or *in vitro/in vivo* micronucleus tests (OECD TG 487/OECD TG 474).

As pointed out under Section '1.1. Reliability of the provided information with analogue substances' under the Appendix on Reasons common to several requests, you have not established the basis of your constituent-based read-across approach. Therefore, it is not clear how you intend to cover the mutagenicity properties of the Substance by using the sources of information on the selected source substances. Due to this major deficiency ECHA cannot assess the relevance and relability of the sources of information provided as part of this weight of evidence against the information requirement stated in the OECD TG 473, 474 and 475 .

Conclusion

It is not possible to conclude, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in *in vitro* cytogenicity study in mammalian cells or in *in vitro* micronucleus study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

In your comments to the draft decision, you agree to perform the requested study.

Information on the study design

To fulfil the information requirement for the Substance, either *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) are considered

suitable.

2. In vitro gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is a standard information requirement in Annex VIII to REACH in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test in mammalian cells or an *in vitro* micronucleus study.

Triggering

Your dossier contains inadequate data for *in vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.) and for *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.), performed with source substances which are rejected for the reasons provided in Appendix A, section 1. and Appendix B, Section 1.

The results of the requests for information in Appendix A, Section 1. and Appendix B, Section 1 will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

Your dossier does not contain any study or adaptation in accordance with column 2 of Annex VIII, Section 8.4.3. or with the general rules of Annex XI for this standard information requirement.

Consequently, you are required to provide information for this endpoint, if the *in vitro* gene mutation study in bacteria / the *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study provides a negative result.

In your comments to the draft decision, you agree to perform the requested study.

Study design

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

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

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

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH (weight of evidence).

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

with p-toluenesulphonic acid (EC: 203-180-0; CAS: 104-15-4):

(i) Short-term (28-day) toxicity study in rats (OECD TG 407, GLP, 1990)

with Sodium xylene sulfonate (EC: 215-090-9; CAS: 1300-72-7):

(ii) Sub-chronic toxicity dietary study in rats (equivalent to OECD TG 408, GLP not specified, 1968)
(iii) Sub-chronic (90-day) toxicity dietary study in rats (equivalent to OECD TG 408, GLP

not specified, 1980)
(iv) Sub-chronic (90-day) toxicity dietary study in mice (no guidance followed, GLP not specified, 1979)
(v) Combined chronic toxicity/carcinogenicity study in rats (similar to OECD TG 453, GLP, NTP)
(vi) Combined chronic toxicity/carcinogenicity study in mice (similar to OECD TG 453, GLP, NTP)

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

Relevant information for this endpoint can be obtained from OECD TG 407/408.

As pointed out under Section '1.1. Reliability of the provided information with analogue substances' under the Appendix on Reasons common to several requests, you have not established the basis of your constituent-based read-across approach. Therefore, it is not clear how you intend to cover the systemic toxicity properties of the Substance by using the sources of information on the selected source substances. Due to this major deficiency ECHA cannot assess the relevance and relability of the sources of information provided as part of this weight of evidence against the information requirement stated in the OECD TG 407/408 guidelines.

In your comments to the draft decision you disagree to perform the requested test on the Substance (UVCB) itself but rather to look for data on the individual constituents. You state that *"Additional studies conducted as per the OECD 407 or OECD 408 (Repeated Dose 90-Day Oral Toxicity Study in Rodents) on the most toxicologically significant individual components of the substance will be sought"* and that the read-across hypothesis will be re-evaluated subsequently.

ECHA acknowledges your intention, however, you have not provided in your comments any new scientific information addressing this information requirement. In the absence of such information, ECHA is not in a position yet to assess or conclude on the compliance of the read across adaptation. You remain responsible for complying with this decision by the set deadline.

Conclusion

It is not possible to conclude, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in OECD TG 407.

Based on the above, the adaptation is rejected and the information requirement is not fulfilled.

Information on the study design

Referring to the criteria in Annex VIII, Section 8.6.1, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity. The Substance is a liquid of very low vapour pressure (0.019 Pa). Uses with spray application (PROC 7) are reported in the chemical safety report. However, the reported the exposure concentrations in the chemical safety report for the inhalation route are low (maximum [redacted] mg/m^3) are low). Therefore the sub-acute toxicity study must be performed according to the OECD TG 407, in rats and with oral administration of the Substance

2. 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 adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5 using the following:

- A study according to OECD TG 203 conducted on p-toluene sulfonic acid (EC: 203-180-0; CAS: 104-15-4) - [redacted] 1981

We have assessed this information and identified the following issues:

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

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6. and related documents[7,8].

You have provided a read-across justification document in IUCLID Section 13, entitled "[redacted]", hereafter "justification document".

You propose to predict the properties of your Substance using data from "[…] *similar substances of the constituents of Phenol, sulfonated*". For the information requirements under consideration, you read-across between the structurally similar substances, p-toluene sulfonic acid, EC No. 203-180-0 (CAS No. 104-15-4) as source substance and the Substance as target substance.

You have provided the following reasoning for the prediction of (eco)toxicological properties: *"Considering the high structural homology and considering the similarity of the substances with the constituents of the UVCB, it could be concluded that it seems reasonable and suitable to perform read-across for the indicated endpoints".*

You consider that *"The chemical structures of the similar substances are comparable to the chemical structure of the constituents of Phenol, sulfonated (UVCB)".*

You further state that *"A category approach based on the main components aromatic sulphonic acids can be taken into account for the hazard evaluation of the whole UVCB substance"* and that *"The studies with the salts (hydrotropes) provide valid read-across for the acids […] therefore the dataset for the entire hydrotropes category can be applied broadly".*

On the basis of this information ECHA understands that you have applied a constituent-based approach whereby you conclude on the properties of the Substance using the results obtained from independent studies conducted with the source substance, structurally similar to the constituents of your UVCB Substance.

ECHA understands that you predict the properties of the Substance using a read-across

[7] Read-across assessment framework (RAAF, March 2017)
[8] RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)

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 shortcoming(s) with regards to prediction(s) of (eco)toxicological properties.

A. For the same reasons explained under Section 1.1 (Missing information on the link between the source substances and the Substance) of the Appendix on 'Reasons common to several requests', your read-across fails for the present endpoint too.

B. Source study is not reliable

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment.

To fulfil the information requirement, a source study must comply with the OECD TG 203. Therefore, the following requirements must be met:

Characterisation of exposure:

- Chemical specific analysis of the test solutions is required to demonstrate stability of exposure concentrations during the test;
- The results can be based on nominal or measured initial concentration only if the concentration of the test material has been maintained within 20 % of the nominal or measured initial concentration throughout the test;

Your registration dossier provides an OECD TG 203 study showing the following:

Characterisation of exposure:

- No analytical measurement of test concentrations was conducted;
- You based the LC50 on nominal concentrations but you did not provide any evidence to demonstrate stability of exposure concentrations during the test.

Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, in the absence of analytical measurement of test concentrations, you have not demonstrated that the exposure concentrations were maintained within 20% of the nominal concentration throughout the duration of the test.

Therefore, the requirements of OECD TG 203 are not met and therefore this study is not adequate for the purpose of classification and labelling and/or risk assessment.

Due to the above, your read-across adaptation under Annex XI, Section 1.5. is rejected. On this basis, the information requirement is not fulfilled.

In your comments to the draft decision, you agree to perform the requested study.

Study design

OECD TG 203 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Section A.2.

Appendix C: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. Test methods, GLP requirements and reporting

1. Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

2. Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[9].

B. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

1. Selection of the Test material(s)

The Test Material used to generate the new data must be selected taking into account the following:

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

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

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

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[10].

[9] https://echa.europa.eu/practical-guides
[10] https://echa.europa.eu/manuals

Appendix D: General recommendations when conducting and reporting new tests for REACH purposes

A. Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituents and, as indicated in ECHA Guidance R.11 (Section R.11.4.2.2), you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach, (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthesize its relevant constituents and/or fractions.

Appendix E: Procedure

The information requirement for a Screening for reproductive/developmental toxicity study (Annex VIII, Section 8.7.1.) is not addressed in this decision due to the on-going harmonised classification and labelling process for one of the components ([redacted]) of the Substance (as Repro 1B). Since the Substance contains [redacted] above ≥0.3% w/w, you must classify your Substance in accordance with section 3.7.3.1.1. of Annex I to the CLP Regulation (EC) No 1272/2008 following the inclusion of [redacted] in Part 3 of Annex VI to that regulation or to provide reasons in your registration dossier for no classification. These reasons should be scientifically justified. The concentration limit of ≥0.3% w/w for Category 1A/1B is given in Table 3.7.2. of Annex I to the CLP Regulation (EC) No 1272/2008.

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 16 July 2020.

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

ECHA took into account your comments and did not amend the request(s).

Deadline to submit the requested information in this decision

In your comments on the draft decision, you requested an extension of the deadline to provide information from 12 to 24 months from the date of adoption of the decision. You considered that the extension of 12 months is needed for the following reasons: first, for the development and validation of a suitable analytical method to verify test concentrations in the aquatic toxicity studies. You claim that such verification of the concentrations will be needed also for the repeated dose toxicity study. Second, you state that you need more time for conducting ready biodegradability tests on the single constituents of the Substance, in case the testing strategy proposed in your comments is not considered acceptable.

ECHA notes that analytical verification of test concentrations is not required for the repeated dose toxicity study. ECHA agrees that in the aquatic toxicity studies analytical monitoring of the test solutions is needed to verify the exposure concentrations. Since the Substance is a UVCB, ECHA acknowledges that extra time may be needed to develop a suitable analytical method and providing an additional 6 months is considered as sufficient for that purpose. Further extension, based on the reasons provided in regard to the repeated dose toxicity and in light of ECHA agreeing with your proposal for biodegradability testing, is considered unjustified.

On this basis, ECHA has extended the deadline by 6 months to 18 months.

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

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

Appendix F: List of references - ECHA Guidance[11] 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)[12]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[12]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[13]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

[11] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[12] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[13] 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 G: Addressees of this decision and their corresponding information requirements

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[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.