EUROPEAN CHEMICALS AGENCY

Helsinki, 12 December 2018

Addressee: [redacted]

Decision number: CCH-D-2114453300-64-01/F
Substance name: Alkane C6-C8 (even numbered), 1-sulphonic acid, sodium salt
EC number: 939-625-7
CAS number: NS
Registration number: [redacted]
Submission number: [redacted]
Submission date: 22/05/2013
Registered tonnage band: 100-1000

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490) with the registered substance;**

2. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: OECD TG 408) in rats with the registered substance;**

3. **Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: OECD 421/422) in rats, oral route with the registered substance;**

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

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

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI to the REACH Regulation. To ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by ***21 June 2021***. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

Appeal

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

Authorised[1] by Kevin Pollard, Head of Unit, Evaluation E1

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

Appendix 1: Reasons

(ECO)TOXICOLOGICAL INFORMATION

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Your registration dossier contains for multiple endpoints adaptation arguments in the form of a grouping and read-across approach under Annex XI, Section 1.5. of the REACH Regulation. ECHA has considered first the scientific and regulatory validity of your read-across approach in general before assessing the individual endpoints (sections 1 to 5).

ECHA does note that in light of the considerations below you have indicated in your comments to the draft decision sent to you on 29 May 2018 that you will remove the read-across data for the human health endpoints. Nevertheless, for the sake of clarity ECHA has kept below its initial reasoning for not accepting the read-across for those end-points.

Grouping of substances and read-across approach

You have sought to adapt information requirements by applying a read-across approach in accordance with Annex XI, Section 1.5, for the endpoints:

- in vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- sub-chronic toxicity (90-day) study (Annex IX, Section 8.6.2.)
- screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.1).

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (read-across approach). ECHA considers that the generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a toxicological or ecotoxicological property is reliable and should be based on recognition of the structural similarities and differences between the source and registered substances[2]. This hypothesis must explain why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures. There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case.

[2] Please see for further information ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6: QSARs and grouping of chemicals.

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

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

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

You consider to achieve compliance with the REACH information requirements for the registered substance alkane C6-C8 (even numbered), 1-sulphonic acid, sodium salt using data of structurally similar substances sodium dodecyl sulfate (EC no 205-788-1), alcohol sulphate (EC no not indicated) and sodium octane-1-sulfonate hydrate (EC no 226-195-4) (hereafter the 'source substances').

You have provided read-across arguments in some of the IUCLID sections, and some of this information, or similar information, is also given in the CSR in the registration dossier. You have, however, not submitted a separate document to justify your category approach.

You use the following arguments to support the prediction of properties of the registered substance from data for source substances within the group:

IUCLID section 6.1.3.:
"Properties of the registered substance are applicable to the test substance, as this substance is the major constituent of the registered substance."

IUCLID section 7.1.:
"The anionic surfactants (ANS) category includes three structurally related classes of substances: Alkyl sulfates, which are sulfate salts consisting of a predominantly linear alkyl chain bearing a terminal sulfate ester anion, neutralised with a base (single chain length or a defined chain length distribution); primary alkane sulfonates, the salt of a linear saturated alkyl chain, bearing a terminal sulfonate anion, neutralized with sodium hydroxide; and alpha-olefin sulfonates, a mixture of sodium alkene sulfonate and hydroxyl alkane sulfonate salts, with the sulfonate group in the terminal position and the double bond, or hydroxyl group, located at various positions along a linear aliphatic chain in the vicinity of the sulfonate group."

[3] Please see ECHA's Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across).

"The most important common structural feature of the category member is the presence of a predominantly linear aliphatic hydrocarbon chain with a polar sulfate or sulfonate group, neutralized with a counter ion."

"Common physical and/or biological pathways result in structurally similar breakdown products and are, together with the surfactant properties, responsible for the essentially identical hazard profiles with regard to human health."
"The toxicological properties of the ANS category were assessed under the high production volume (HPV) chemicals program of the Organisation for Economic Cooperation and Development (OECD) in 2007 ..... using a category approach (a grouped approach, in which data for individual members are presented and discussed together as part of a category, rather than substance-by-substance)."

"For those members of the category where reliable data were not available for all obligatory endpoints required according to the Manual for Investigation of HPV Chemicals, read across of toxicological data from closely related chemicals of the category was applied to address their properties."

"After absorption, these chemicals are distributed mainly to the liver and the alkyl sulfates, alkane sulfonates and most probably also alpha-olefin sulfonates are metabolized by cytochrome P450-dependent omega-oxidation and subsequent beta-oxidation of the aliphatic fatty acids. End products of the oxidation are a C4 sulfate or sulfonate (even numbered chain lengths) and a C3 or C5 sulfate or sulfonate (odd numbered chain lengths)."

"Several reasons for a lack of concern regarding bioaccumulation exist including rapid excretion of metabolites via urine, limited dermal exposure (main route of consumer exposure) and the low concentration of substances in consumer products."

IUCLID section 7.5.:
"The toxicological profile of the alkyl sulfates and the alkane sulfonates reveals many similarities. For all compounds where data are available, the acute oral toxicity as well as repeated oral toxicity is low. After multiple oral dosing, the gastrointestinal tract (dosing via gavage), and the liver were identified as target organs. The similarity between both subgroups is evident also for other endpoints such as skin and eye irritation, sensitization, mutagenicity, carcinogenicity and reproductive and developmental toxicity. Longer-term studies as well as data concerning carcinogenicity or reproduction toxicity are missing. However, based on metabolism studies it can be concluded that the properties of the alkyl sulfates and sulfonates are similar."

IUCLID section 7.8.:
"There are no reproductive toxicity studies available for either alkyl sulfates or alkane sulfonates that have been performed to standard protocols. A study available for C12 alkyl sulfate showed no adverse effects on epididymal spermatozoa and derived a NOAEL for male fertility of 1000 mg/kg bw/day. The results of several 90-day repeated dose toxicity studies performed using higher chain length alkyl sulfates gave no indication for adverse effects on reproductive organs at histopathological examinations."
As an integral part of this prediction, you propose that the source and registered substance(s) have similar properties for the above-mentioned information requirements. ECHA considers that this information is your read-across hypothesis.

ECHA's evaluation and conclusion

ECHA considers that the suggested category cannot be accepted as category boundaries and category membership criteria have not been provided. Therefore, ECHA assessment below has been conducted as for endpoint-to-endpoint read-across adaptations.

Your proposed adaptation argument is that the similarity in chemical structure and in some of the ecotoxicological and toxicological properties between the source and registered substance is a sufficient basis for predicting the properties of the registered substance for other endpoints. Structural similarity is a prerequisite for applying the grouping and read-across approach. However similarity in chemical structure and similarity of some of the ecotoxicological and toxicological properties does not necessarily imply that human health/environmental properties in other endpoints can be predicted.

Regarding the structural similarity of the substances, you claim, for example, that the source substance sodium octane-1-sulfonate hydrate (EC no 226-195-4) is a major constituent of the registered substance. In your technical dossier the concentration range for this constituent is given at [redacted]. Hence, it remains to be demonstrated whether and how the remaining constituents of the target substance would influence the (eco)toxicological properties of the substance. Furthermore, ECHA notes that two of the selected source substances are sodium salts of alkyl sulfates/ alkohol sulphates and not alkane sulfonates. The potential differences in the hazardous properties linked to the differences in functional groups have not been addressed in your read-across justification.

Furthermore, regarding similarity of (eco)toxicological properties, ECHA notices that you have not made a detailed comparison of the hazard profiles of the target and the source substances, and there is, for example, no data matrix submitted to support your read-across (please see further the "Read-Across Assessment Framework"[4]). Your provided arguments have not established why predictions would be reliable for the human health/ environmental end-points, for which the read-across is claimed.

Additionally, ECHA has taken into account all of your arguments together. ECHA firstly notes that you have not provided a reasoning as to why these arguments add to one another to provide sufficient basis for read-across. Secondly, the defects of each individual argument are not mitigated by the other arguments you have provided, and so ECHA considers that the arguments when taken all together do not provide a reliable basis for predicting the properties of the registered substance.

Therefore, ECHA considers that this grouping and read-across approach does not provide a reliable basis whereby the human health effects or environmental effects of the registered substance may be predicted from data for reference substance(s) within the group. Hence, this approach does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. of the REACH Regulation. ECHA notes that there are specific considerations for the individual endpoints which also result in a failure to meet the requirement of Annex XI, Section 1.5., and these are set out under the endpoint concerned.

ECHA's evaluation of your comments to the draft decision

In your comments on the draft decision you indicate that you will remove the read-across data for the following endpoints and conduct new studies on the registered substance to fill the data gaps: in vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.); sub-chronic toxicity (90-day) study (Annex IX, Section 8.6.2.); and pre-natal developmental toxicity study (Annex IX, Section 8.7.2.).

You further indicated that you have revised the read-across justification for short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.1). Indeed, you include an analogue approach justification for this information requirement, and you conclude that read-across from the data available on the analogue substance sodium octane-1-sulfonate hydrate (EC No 226-195-4; CAS No 5324-84-5) may be supported.

ECHA notes that the provided justification includes a data matrix with physico-chemical and ecotoxicological characteristics of both substances, target and source substances. You mention that the Consistency of properties of the data matrix is good (A.4) and "*The acute algae toxicity studies for both substances support the low toxicity of these substances to the aquatic environment*". You further state under "*Common underlying mechanism, quantitative aspects*" (2.4) that "*The only available ecotoxicity that is common between the substances is the acute toxicity to algae study. In both studies the ErC50 was reported as > 100 mg/L (nominal). These studies support the proposal that the acute aquatic toxicity of these substances is low*". In the results on Growth inhibition study on algae, the source substance NOErC=100 mg/L (used test concentrations are 0.954, 3,05, 9.77, 31.3, 100, 1000 mg/L), while in the test with the target substance NOErC=6.25 mg/L (used test concentrations are 6.25; 12.5; 25; 50 and 100 mg/L). Thus, the toxicity of the target substance on algae growth seems to be higher than that of the source substance. Hence, the only available ecotoxicity data that is common between the substances seem to show different sensitivity to these two substances. Thus, ECHA concludes that you have not demonstrated that the substances have similar ecotoxicological properties.

Overall, ECHA concludes that the provided justification does not demonstrate the suitability of the read across from the data available on sodium octane-1-sulfonate hydrate (EC No 226-195-4; CAS No 5324-84-5) to your registered substance.

As described above, further elements are needed to establish a reliable prediction for a toxicological or ecotoxicological property, based on recognition of the structural similarities and differences between the source and registered substances. This could be achieved (if it is possible) by a well-founded hypothesis of (bio)transformation to a common compound(s), or that the registered and source substance(s) have the same type of effect(s), together with sufficient supporting information to allow a prediction of human health/environmental properties.

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

An "*In vitro* gene mutation study in mammalian cells" is an information requirement as laid down in Annex VIII, Section 8.4.3. of the REACH Regulation, "if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2." is obtained. Therefore, adequate information *on in vitro* gene mutation in mammalian cells needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation [by providing (a) study record(s) for an "in vitro gene mutation study in mammalian cells" (OECD TG 476) with the analogue substance(s) sodium dodecyl sulfate (EC no 205-788-1).

However, as explained above in Appendix 1, section "Grouping of substances and read-across approach" of this decision, your adaptation of the information requirement according to Annex XI, Section 1.5. is rejected.

In your comments to the draft decision notified to you on 29 May 2018, you indicated that the read across substance used in the dossier to address this endpoint is no longer considered sufficiently similar enough to be used in filling this data requirement and that therefore you will remove the read across substance from the dossier and fill the data gap with a study of the registered substance.

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

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

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *In vitro* mammalian cell gene mutation test (test method: OECD TG 476 *or* OECD TG 490).

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

A "sub-chronic toxicity study (90 day)" is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided a study record for a "short-term repeated dose toxicity" (test method: OECD TG 407, exposure for 14 days) with the registered substance. However, this study does not provide the information required by Annex IX, Section 8.6.2., because exposure duration is less than 90 days and the number of animals per dose group is significantly lower than in the 90 day sub-chronic toxicity study (OECD TG 408) . Therefore, the sensitivity of a 14-day study is much lower than that of a 90-day study.

You have also sought to adapt this information according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a "sub-chronic toxicity study" in rat, oral route (comparable to OECD TG 408) with the analogue substance sodium dodecyl sulfate (EC no 205-788-1).

However, as explained above in Appendix 1, section "Grouping of substances and read-across approach" of this decision, your adaptation of the information requirement according to Annex XI, Section 1.5. is rejected.

In your comments to the draft decision notified to you on 29 May 2018, you indicated that the read across substance used in the dossier to address this endpoint is no longer considered sufficiently similar enough to be used in filling this data requirement and that therefore you will remove the read across substance from the dossier and fill the data gap with a study of the registered substance.

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

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 5.0, December 2016) Chapter R.7a, Section R.7.5.4.3 - is the most appropriate route of administration. More specifically, even though the information indicates that human exposure to the registered substance by the inhalation route is likely, you indicate that *"The substance is a solid with very low vapour pressure. It is manufactured and supplied as* [redacted]*, therefore there is no possibility of exposure to dust. It is used in* [redacted]*, but it is expected that inhalation exposure from these applications will be low."* Hence, the test shall be performed by the oral route using the test method OECD TG 408.

According to the test method OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Repeated dose 90-day oral toxicity study (test method: OECD TG 408) in rats.

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

"Screening for reproductive/developmental toxicity" (test method OECD TG 421 or 422) is a standard information requirement as laid down in Annex VIII, Section 8.7.1. of the REACH Regulation if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from *in vitro* methods that the substance may be a developmental toxicant. No such evidence is presented in the dossier. Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a screening for reproductive/developmental toxicity in the dossier that would meet the information requirement of Annex VIII, Section 8.7.1. Instead you have provided the following adaptation:

"Based on the assessment of the toxicological properties of the anionic surfactants (ANS) category performed under the high production volume (HPV) chemicals program of the Organisation for Economic Cooperation and Development (OECD) in 2007 at the OECD SIDS Initial Assessment Meeting (SIAM) 25 there are no reproductive toxicity studies available for either alkyl sulfates or alkane sulfonates that have been performed to standard protocols. In one older study [[redacted]*(1981)] groups of 10 male Swiss albino mice were dosed orally with either 1% of C12 ASO4 Na for 2 weeks or with 0.1% of C12 ASO4 Na for 6 weeks and 1–3 weeks after dosing the animals of each group were mated. The treatment caused no adverse effects on epididymal spermatozoa, and from this study a NOAEL for male fertility of 1000 mg a.i./kg bw/day can be derived. The results of several repeated oral dose 13-week studies with C12–15 ASO4 Na, C16–18 ASO4 Na, and C13–15 ASO4 Na gave no indication for adverse effects on reproductive organs at the histopathological examinations. Although at very high doses (>1000 mg/kg bw/day) increases in relative (but not absolute) testes weights were noted, this effect is not considered as adverse but can be attributed to a decrease in body fat and bodyweight [OECD (2007)]. In an extended 14-day repeated dose range finding study, C6 -8 alkane sulfonate was administered daily by gavage to CD® rats [*[redacted]*(2013)]. The rats were treated with 100, 300 or 1000 mg/kg bw/day. None of the animals died prematurely. All animals treated with 100, 300 or 1000 mg/kg bw/day*

revealed salivation immediately after administration that lasted for 10 to 15 minutes on up to 5 test days starting on test day 2. No test item-related influence was noted on body weight and body weight gain, food and drinking water consumption, haematological and biochemical parameters. Treatment with 1000 mg/kg b. w. /day resulted in a slight increase in the relative and absolute weight of the stomach (statistically not significant at p<0.01). The macroscopic post mortem examination did not reveal any test item-related changes at any dose level including in gonads, uterus and accessory reproductive organs. Therefore on the basis of read across to the available data on alkyl sulfates, supported by the findings in the 14-day study with the substance itself, adverse effects on fertility are not expected and testing is scientifically unjustified. References [redacted] *(1981) Male mouse fertility after ingestion of spermicidal detergents. Soc. Occup. Med. 9, 243–244. OECD (2007) Category of Alkyl sulfates, Alkane sulfonates and a-Olefin sulfonates. SIDS Initial Assessment Report for SIAM 25, Organization for Economic Cooperation and Development, Paris. OECD Integrated HPV database online at /http://cs3-hq.oecd.org/scripts/hpvS. Wibbertmann A, Mangelsdorf I, Gamon K, Sedlak R (2011) Toxicological properties and risk assessment of the anionic surfactants category: Alkyl sulfates, primary alkane sulfonates, and alpha-olefin sulfonates, Ecotoxicology and Environmental Safety, 74, 1089–1106"*

In support of the adaptation you have submitted the following study records:

- Weight of evidence (section 7.5.1 in IUCLID): "short-term repeated dose toxicity: oral" in rat, oral route (OECD TG 407 with 14 days of exposure; GLP) with the registered substance, [redacted], 2013 (study report), rel. 1.
- Weight of evidence (section 7.5.1 in IUCLID): "sub-chronic toxicity: oral" in rat, oral route (comparable to OECD TG 408; pre-GLP) with the analogue substance sodium dodecyl sulfate (EC no 205-788-1), Walker et al., 1967 (publication), rel. 2.

ECHA has first evaluated your adaptation according to Annex XI, Section 1.5. of the REACH Regulation (Grouping of substances and read-across). However, as explained above in Appendix 1, section "Grouping of substances and read-across approach" of this decision, your adaptation of the information requirement according to Annex XI, Section 1.5. is rejected. ECHA also notes that the study by [redacted] (1981) referred to in your adaptation (but not submitted in your IUCLID dossier) would not fulfil the standard requirements for this endpoint as it only investigated effects on reproduction in male animals.

As the read-across is rejected, ECHA evaluated the available study conducted using the registered substance, together with your justification for the adaptation, according to Annex XI, Section 1.2 (Weight of evidence).

An adaptation pursuant to Annex XI, Section 1.2. requires sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property with respect to the information requirement in question including an adequate and reliable documentation.

Your weight of evidence adaptation needs to address the specific dangerous (hazardous) properties of the registered substance with respect to the effects of the substance on male and female reproductive performance. The 14-day repeated dose toxicity study with the registered substance ([redacted] 2013) referred to in your adaptation did not include mating of the animals, and no information was for that reason obtained related to reproductive performance.

Moreover, the study conducted with sodium dodecyl sulfate (EC no 205-788-1) cannot be considered as evidence for the same reasons as explained above for the rejection of the read-across from the proposed source substance.

Hence, the sources of information you provided, together with your justification for the adaptation, do not allow to assume/conclude that the substance does not have a particular dangerous (hazardous) property with respect to the information requirement for Annex VIII, Section 8.7.1.

In your comments to the draft decision notified to you on 29 May 2018, you indicate that the read across substance used in the dossier to address this endpoint is no longer considered sufficiently similar enough to be used in filling this data requirement and will be removed from the dossier. You further indicate that a "screening for reproductive/ developmental toxicity" study is not necessary according to Annex VIII column 2 if there is a "pre-natal developmental toxicity study" (OECD TG 414) available and that this therefore makes the OECD 421 or OECD 422 study unnecessary. ECHA agrees with the comment but has kept the request as there is currently no "pre-natal developmental toxicity study" available for the registered substance. ECHA notes however your agreement to perform the pre-natal developmental toxicity study and that the information requirement for a screening study can indeed be fulfilled by the provision of the pre-natal developmental toxicity study.

Therefore, the general rules for adaptation laid down in Annex XI, Section 1.2. of the REACH Regulation are not met and your adaptation of the information is rejected.

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

According to the test methods OECD TG 421/422, the test is designed for use with rats. On the basis of this default assumption ECHA considers testing should be performed with rats.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid, ECHA concludes that testing should be performed by the oral route.
Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Reproductive/developmental toxicity screening test (test method: OECD TG 421) *or* Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (test method: OECD TG 422) in rats by the oral route.

Notes for your considerations

You should carefully consider the order of testing of the requested screening (OECD TG 421/422) and the developmental toxicity studies (OECD TG 414) to ensure that unnecessary animal testing is avoided, paying particular attention to the endpoint specific guidance
(https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf) Section R.7.6.2.3.2., pages 484 to 485 of version 6.0 – July 2017."

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

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

You have sought to adapt this information according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a "developmental toxicity study" (OECD TG 414) with the analogue substance alcohol sulphate (EC no not indicated).

However, as explained above in Appendix 1, section "Grouping of substances and read-across approach" of this decision, your adaptation of the information requirement according to Annex XI, Section 1.5. is rejected.

In your comments to the draft decision notified to you on 29 May 2018, you indicated that the read across substance used in the dossier to address this endpoint is no longer considered sufficiently similar enough to be used in filling this data requirement and that therefore you will remove the read across substance from the dossier and fill the data gap with a study of the registered substance.

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

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

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

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: OECD TG 414) in a first species (rat or rabbit) by the oral route.

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

"Short-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex VII, Section 9.1.1. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

Column 2 of Annex VII, Section 9.1.1 specifies that a long-term aquatic toxicity study on Daphnia (Annex IX, section 9.1.5) shall be considered if the substance is poorly water soluble.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a Short-term toxicity to aquatic invertebrates (OECD TG 202) with the analogue substance(s) sodium octane-1-sulfonate hydrate (CAS no 5324-84-5 /EC no 226-195-4).

However, as explained above in Appendix 1, section "Grouping of substances and read-across approach" of this decision, your adaptation of the information requirement cannot be accepted.

In your comments to the draft decision notified to you on 29 May 2018 you included an analogue approach justification for this endpoint. The provided justification does not demonstrate the suitability of the read across from the data available on sodium octane-1-sulfonate hydrate (EC No 226-195-4; CAS No 5324-84-5). (See ECHA's response under "Grouping of substances and read-across approach" section in this decision, above).
As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

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

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *Daphnia* sp. Acute immobilisation test, EU C.2./OECD TG 202).

Notes for your consideration

Due to the surface activity of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 REV1 (6 July 2018) and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 01 March 2018.

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

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

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 took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

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

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In carrying out the tests required by the present decision, it is important to ensure that the particular sample of substance tested is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported. If the registration of the substance covers different grades, the sample used for the new tests must be suitable to assess these.

   Furthermore, there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.