Decision number: CCH-D-2114305285-57-01/F Helsinki, 11 September 2015

DECISION ON A COMPLIANCE CHECK OF A REGISTRATION PURSUANT TO ARTICLE 41(3) OF REGULATION (EC) NO 1907/2006

For sodium prop-2-enesulphonate, CAS No 2495-39-8 (EC No 219-676-5), registration number: [redacted]

Addressee: [redacted]

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

I. Procedure

Pursuant to Article 41(1) of the REACH Regulation ECHA has performed a compliance check of the registration for sodium prop-2-enesulphonate, CAS No 2495-39-8 (EC No 219-676-5), submitted by [redacted] (Registrant). The scope of this compliance check is limited to the standard information requirements of Annex IX, Sections 8.6.2. and 8.7.2. of the REACH Regulation. ECHA stresses that it has not checked the information provided by the Registrant and other joint registrants for compliance with requirements regarding the identification of the substance (Section 2 of Annex VI).

This decision is based on the registration as submitted with submission number [redacted], for the tonnage band of 1000 tonnes or more per year. This decision does not take into account any updates submitted after 05 March 2015, the date upon which ECHA notified its draft decision to the Competent Authorities of the Member States pursuant to Article 51(1) of the REACH Regulation.

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

The compliance check was initiated on 4 November 2013.

On 10 July 2014 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

On 8 August 2014 ECHA received comments from the Registrant on the draft decision. The compliance check requirement to submit information of a two-generation reproductive toxicity study (EU B.35, OECD TG 416) or an extended one-generation reproductive toxicity study (EU B.56, OECD TG 443) has been removed from this draft decision due to the legislative amendments to the REACH Regulation regarding Annex X, Section 8.7.3. In light of this, ECHA Secretariat did not consider further the Registrant's comments concerning the information requirement of Annex X, Section 8.7.3. However, ECHA Secretariat did consider further the Registrant's comments concerning the information requirements of Annex IX, Sections 8.6.2. and 8.7.2. On the basis of all this information, Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

The present draft decision relates solely to a compliance check requesting information in the form of a sub-chronic toxicity study (90-day) and a pre-natal developmental toxicity study (Annex IX, Sections 8.6.2. and 8.7.2.).

On 5 March 2015 ECHA notified the Competent Authorities of the Member States of its draft decision and invited them pursuant to Article 51(1) of the REACH Regulation to submit proposals for amendment of the draft decision within 30 days of the receipt of the notification.

Subsequently, a proposal for amendment to the draft decision was submitted.

On 10 April 2015 ECHA notified the Registrant of the proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on the proposal for amendment within 30 days of the receipt of the notification.

The ECHA Secretariat reviewed the proposals for amendment received and did not amend the draft decision.

On 20 April 2015 ECHA referred the draft decision to the Member State Committee.

By 11 May 2015 the Registrant did not provide any comments on the proposals for amendment.

A unanimous agreement of the Member State Committee on the draft decision was reached on 26 May 2015 in a written procedure launched on 13 May 2015.

ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Information required

Pursuant to Articles 41(1), 41(3), 10(a)(vi) and/or (vii), 12(1)(e), 13 and Annex IX of the REACH Regulation the Registrant shall submit the following information using the indicated test methods and the registered substance subject to the present decision:

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, 8.6.2.; test method: EU B.26./OECD 408) in rats;

2. Pre-natal developmental toxicity study (Annex IX, 8.7.2.; test method: EU B.31./OECD 414) in rats or rabbits, oral route.

Pursuant to Article 41(4) of the REACH Regulation the Registrant shall submit the information in the form of an updated registration to ECHA by **18 September 2017**, including, where relevant, an update of the Chemical Safety Report. The timeline has been set to allow for sequential testing as appropriate.

Note for consideration by the Registrant:

The Registrant 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 of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring to and conforming with the appropriate rules in the respective Annex, and an adequate and reliable documentation.

Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

III. Statement of reasons

Pursuant to Article 41(3) of the REACH Regulation, ECHA may require the Registrant to submit any information needed to bring the registration into compliance with the relevant information requirements.

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) of the REACH Regulation, a technical dossier for a substance manufactured or imported by the Registrant in quantities of 1000 tonnes or more per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, 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.

The Registrant has sought to adapt this information requirement. The justification of the adaptation given by the Registrant is that "In accordance with column 2 of REACH Annex IX, a subchronic toxicity study does not need to be conducted as no evidence of toxicity appeared in a combined study for repeated dose and reproductive/ developmental toxicity in doses up to the limit dose of 1000 mg/kg be/day. Therefore, no further information about the repeated dose toxicity are expected in a subchronic study."

In their comments, the Registrant also referred to REACH Annex XI, 1.2., and stated: "But nevertheless as the highest applied dosage (1000mg/kg; limit dose) in the OECD 422 study reveals no effects nor any indication for substance related finding a further increase of the exposure duration is assumed to shown no additional effects. Therefore this OECD 422 is judged as a reliable source of nearly all data which is normally received from a subchronic or subchronic equivalent study. Consequently no further subchronic study is proposed as sufficient weight of evidence for the absence of a particular dangerous property is available (according to Annex XI, 1.2)". The Registrant also referred to column 2 provisions "Taken together the registrant thinks that all criteria fulfilled to make the adaption according to Annex IX, 8.6.2., column 2 or Annex IX, 8.7.2., column 2 and according to Annex XI, 1.2 and has therefore not proposed any further study."

ECHA notes, firstly, that a combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test (test method: OECD 422) does not provide the information required by Annex IX, Section 8.6.2., because exposure duration is less than 90 days.

Secondly, with reference to the adaptation possibility of Annex IX, 8.6.2., column 2 of the REACH Regulation, ECHA notes that according to this provision the sub-chronic toxicity study does not need to be conducted if the following cumulative conditions are met: (i) the substance is unreactive, insoluble and not inhalable and (ii) there is no evidence of absorption and (iii) no evidence of toxicity in a 28-day 'limit test', particularly if such a pattern is coupled with limited human exposure.
Whereas in the current case no evidence of toxicity was found in the "combined repeated

dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD 422), the test substance is highly water soluble (714 g/L) and there is evidence of absorption, as demonstrated by mortality in an acute oral toxicity study provided by the Registrant in the registration dossier.

The Registrant in their comments consider the death of one animal in the acute oral toxicity study as accidental and also refers to physico-chemical properties of the registered substance (high solubility combined with high hydrophilic property) and their implication on uptake from the GI tract, concluding that the GI absorption is assumed to be small.

ECHA notes that the acute toxicity study shows findings (sporadic dyspnoea, apathy and diarrhoea in the first hours after administration of the high dose of the test substance) that provide some evidence of bioavailability/absorption, as is also stated in the endpoint study summary on toxicokinetics in the dossier (IUCLID item 7.1). Moreover, the Registrant agrees in their comment that there is absorption of the substance, although only limited, and that the possibility of passive diffusion from the GI tract cannot be excluded.

Based on the information summarised above, ECHA notes that conditions (i) and (ii) of this adaptation possibility are not met and the Annex IX, 8.6.2., column 2 adaptation of the information requirement suggested by the Registrant cannot be accepted.

Thirdly, with reference to adaptation possibility of Annex XI, 1.2. of the REACH Regulation (weight of evidence), ECHA notes that for using this adaptation possibility the legal text explicitly requires a 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, while the information from each single source alone is regarded insufficient to support this notion.

The Registrant however provides only one source of information (the OECD 422 study) for the endpoint sub-chronic toxicity. As already outlined above, this single source of information is regarded as insufficient to conclude on toxicity after administration of the substance for 90 days, because exposure duration is less than 90 days. Furthermore, the Registrant did not provide additional sources of information as required for a weight of evidence approach. Thus the conditions of Annex XI, 1.2., are not met, and the adaptation according to Annex XI, 1.2., cannot be accepted.

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

In light of the physico-chemical properties of the substance (solid with low vapour pressure, marketed in a non-solid or granular form, not classified as corrosive/irritating to the skin and/or damaging/irritating to the eyes), ECHA considers that testing by the oral route is most appropriate.

According to the test method EU B.26./OECD 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, the Registrant is 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: EU B.26./OECD 408) in rats.

2. Pre-natal developmental toxicity study (Annex IX, 8.7.2.)

A "pre-natal developmental toxicity study" 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.

The Registrant has sought to adapt this information requirement. The justification of the adaptation given by the Registrant is that "In accordance with column 2 of REACH Annex IX, studies for reproductive toxicity do not need to be conducted as a very low toxicological activity was documented in a combined study for repeated dose and reproductive/ developmental toxicity in doses up to the limit dose of 1000 mg/kg be/day. Therefore, no further information about the reproductive toxicity are expected in a developmental toxicity study."

In their comments, the Registrant also referred to REACH Annex XI, 1.2., and stated: "But the additional information received from a teratogenicity is limited if already not toxicity or hints for toxicity are already seen in another reproduction toxicity study. The OECD 414 is majorly designed to increase the applied dose as far as possible using a shorter duration with the focus to increase the dosage during critical stages of pregnancy. The focus is here to ensure that no malformation / development effects may be triggered by the substance. As the substance was applied in the maximum concentration in a OECD 422 for a longer time period and no malformation or other effects were seen in the pups or the parents additional information of a special examination (direct section after cesarean birth) within the OECD 414 may be very limited." The Registrant also argued that "all pups are born, no unexpected missing happened, which may lead to malformation and cannibalism and that all pups were examined at the end (day 4 after delivery). As there were no abnormalities detected in any pup at necropsy, it can be assumed that also a maximum dosage in a 414 (which is also 1000mg/kg but for a shorter period) will not show any other results." The Registrant also argues "Taken together the registrant thinks that all criteria fulfilled to make the adaption according to Annex IX, 8.6.2., column 2 or Annex IX, 8.7.2., column 2 and according to Annex XI, 1.2 and has therefore not proposed any further study."

ECHA notes, firstly, that a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (test method: OECD 422) does not provide the information required by Annex IX, Section 8.7.2., because it does not cover key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations.

Secondly, ECHA notes that according to Annex IX, 8.7.2., column 2 of the REACH Regulation the study does not need to be conducted if the following cumulative conditions are met: (i) the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), (ii) it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and (iii) there is no or no significant human exposure.

However, these cumulative conditions for adaptation of Annex X, 8.7., column 2 are not met in the current case. Whereas no evidence of toxicity was found in the "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD 422), there was mortality in an acute oral toxicity study provided by the

Registrant in the registration dossier. Several findings in this acute toxicity study (sporadic dyspnoea, apathy and diarrhoea in the first hours after administration of the high dose of the test substance) provide evidence of toxicity. Therefore it cannot be claimed that there is no evidence of toxicity seen in the tests available, and consequently the first criterion is not met. Furthermore, the second criterion is not met, because absorption, although limited, is to be expected, as also agreed by the Registrant in their comments. Moreover, the systemic toxicity seen in the acute toxicity study is also evidence that the substance was absorbed. The parent substance as well as potential metabolites are expected to be excreted via the urine, as stated by the Registrant in IUCLID section 7.1, Toxicokinetics, metabolism and distribution. Furthermore, the Registrant did not prove from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air).

Therefore, the cumulative conditions of the above listed column 2 adaptation possibility are not met and the adaptation of the information requirement suggested by the Registrant cannot be accepted.

Thirdly, with reference to adaptation possibility of Annex XI, 1.2., of the REACH Regulation (weight of evidence), ECHA notes that for using this adaptation possibility the legal text explicitly requires a 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, while the information from each single source alone is regarded insufficient to support this notion.

ECHA notes that the Registrant provides only one source of information (the OECD 422 study) for the endpoint pre-natal developmental toxicity. However, this single source of information is regarded as insufficient to conclude on pre-natal developmental toxicity of the substance, because it does not cover key parameters of a pre-natal developmental toxicity study like e.g. examination of the foetuses for skeletal alterations. Furthermore, the Registrant did not provide additional sources of information as required for a weight of evidence approach. Thus the conditions of Annex XI, 1.2., are not met, and the adaptation according to Annex XI, 1.2., cannot be accepted.

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

According to the test method EU B.31/OECD 414, the rat is the preferred rodent species, the rabbit the preferred non-rodent species and the test substance is usually administered orally. ECHA considers these default parameters appropriate and testing should be performed by the oral route with the rat or the rabbit as a first species to be used.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, the Registrant is requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD 414) in rats or rabbits by the oral route.

In addition, a pre-natal developmental toxicity study on a second species is part of the standard information requirements as laid down in Annex X, Section 8.7.2. for substances registered for 1000 tonnes or more per year (see sentence 2 of introductory paragraph 2 of Annex X).

The Registrant should firstly take into account the outcome of the pre-natal developmental toxicity on a first species and all other relevant available data to determine if the conditions are met for adaptations according to Annex X, 8.7. column 2, or according to Annex XI; for example if the substance meets the criteria for classification as toxic for reproduction Category 1B: May damage the unborn child (H360D), and the available data are adequate to support a robust risk assessment, or alternatively, if weight of evidence assessment of all relevant available data provides scientific justification that the study in a second species is not needed. If the Registrant considers that testing is necessary to fulfill this information requirement, he should include in the update of his dossier a testing proposal for a pre-natal developmental toxicity study on a second species. If the Registrant comes to the conclusion that no study on a second species is required, he should update his technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex X, 8.7.2.

Deadline for submitting the required information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 36 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also contained a two-generation reproductive toxicity study (EU B.35, OECD TG 416) or an extended one-generation reproductive toxicity study (EU B.56, OECD TG 443) (Annex X, Section 8.7.3.). As these studies are not addressed in the present decision, ECHA Secretariat considers that a reasonable time period for providing the required information in the form of an updated IUCLID5 dossier is 24 months from the date of the adoption of the decision. The decision was therefore modified accordingly.

IV. Adequate identification of the composition of the tested material

ECHA stresses that the information submitted by the Registrant and other joint registrants for identifying the substance has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation . The Registrant is reminded of his responsibility and that of joint Registrants to ensure that the joint registration covers one substance only and that the substance is correctly identified in accordance with Annex VI, Section 2 of the REACH Regulation.

In relation to the information required by the present decision, the sample of substance used for the new studies must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is within the specifications of the substance composition that are given by the joint registrants. It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition.

In addition, it is important to ensure that the particular sample of substance tested in the new studies 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 by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new studies must be suitable to assess these grades.

Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the studies to be assessed.

V. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Article 51(8) of the REACH Regulation. Such an appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on ECHA's internet page at http://www.echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

Authorised[1] by Guilhem de Seze, Head of Unit, Evaluation

[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.