Helsinki, 5 July 2016

Addressee: [redacted]

Decision number: CCH-D-2114333681-53-01/F
Substance name: sodium sulphamidate
EC number: 237-572-8
CAS number: 13845-18-6
Registration number: [redacted]
Submission number: [redacted]
Submission date: 5 December 2012

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. The assessment performed for the skin irritation endpoint (standard information requirement as specified in Annex VII, 8.1.) on the registered substance, on which basis an *in vivo* skin irritation study was performed in accordance with Annex VIII, section 8.1.;

2. The assessment performed for the eye irritation endpoint (standard information requirement as specified in Annex VII, 8.2.) on the registered substance, on which basis an in vivo eye irritation study was performed in accordance with Annex VIII, section 8.2.;

3. Justification for performing, on the registered substance, the Guinea Pig Maximisation Test (EU method B.6/OECD 406) instead of the Local Lymph Node Assay (EU method B.42/OECD 429), as specified in Annex VII, 8.3, column 2.

You are required to submit the requested information in an updated registration dossier by **12 January 2017**. You shall also update the chemical safety report, where relevant.

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

The scope of this compliance check is limited to the standard information requirements of Annexes VII and VIII, sections 8.1 to 8.3 of the REACH Regulation.

Appeal

[For the final decision: 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, shall 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/web/guest/regulations/appeals.]

Authorised[1] by Ofelia Bercaru, Head of Unit, Evaluation E3

[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

1. The assessment performed for the skin irritation endpoint (standard information requirement as specified in Annex VII, 8.1.) on the registered substance, on which basis an *in vivo* skin irritation study was performed in accordance with Annex VIII, section 8.1.

According to Article 41(1)(a) of the REACH Regulation, ECHA may verify whether the information submitted by registrants was generated in compliance with the requirements of Articles 10, 12 and 13 of the REACH Regulation and with Annexes III and VI to X.

Pursuant to Article 13(1) of the REACH Regulation in particular information on human toxicity shall be generated whenever possible by means other than vertebrate animal tests, through the use of alternative methods, for example *in vitro* methods.

The introductory note to Annex VI provides that "*the precise information requirements will differ, according to tonnage, use and exposure, and the requirements of the corresponding Annex have to be considered in addition to the prior Annexes. The Annexes shall thus be considered as a whole, and in conjunction with the overall requirements of registration, evaluation and the duty of care*". Furthermore, as specified in the first paragraph of the introductory note of Annex VIII the information required under column 1 of Annex VIII is additional to that required in column 1 of Annex VII. Moreover, according to the third paragraph of that note, before new tests are carried out all available information (including *in vitro* data) shall be assessed first.

With a view to skin irritation, according to Annex VII, 8.1 to the REACH Regulation, the assessment of the endpoint shall comprise, consecutively, an assessment of the available human and animal data, an assessment of the acid or alkaline reserve, an *in vitro* study for skin corrosion, and an *in vitro* study for skin irritation.

According to the Annex VIII, section 8.1., an *in vivo* skin irritation study is a standard information requirement. ECHA's Guidance on information requirements and chemical safety assessment further provides that for substances registered at above 10 tonnes the *in vivo* study for skin corrosion/irritation should be provided, in case the information requirement cannot be met with the information obtained as specified in section 8.1 of Annex VII (See guidance R.7a, chapter R.7.2.2.2 (July 2015)). In particular the guidance states as follows:

> "*Before new tests are carried out to determine the properties listed in Annex VIII, all available in vitro data, in vivo data, historical human data, data from valid (Q)SARs and data from structurally related substances (read-across approach) must be assessed first. Due to the sequential nature of the REACH standard information requirements, the reader is reminded that at quantities of ≥10 tpa, the information requirements of Annex VII to the REACH Regulation also apply. This means that before a new in vivo test is performed, the appropriate in vitro testing must be undertaken according to the rules set out in section 8.1 of Annex VII and must be documented in the technical dossier (IUCLID). Finally, the information generated at Annex VII level must be taken into account in determining whether an in vivo test at Annex VIII level is really needed*".

ECHA notes that you have provided an *in vivo* skin irritation study according to EU method B.4/OECD 404 performed between 23 June and 8 July 2011 in order to fulfil the information requirement for Annex VIII, section 8.1.

However, the registration dossier does not document the information that should have been generated in accordance with Annex VII, section 8.1. Furthermore, the registration dossier does not show how information required under Annex VII section 8.1 was taken into account in determining the need for the *in vivo* test. Accordingly, the relevant assessment required under Annex VII, section 8.1 is missing in the registration dossier and therefore does not enable ECHA to determine how you have complied with the requirement in Article 13(1) of the REACH Regulation to generate information whenever possible by means other than vertebrate animal tests.

In your comments to the draft decision, you did not provide any further information on the assessment of information in accordance with Annex VII, section 8.1, but instead indicated regulatory requirements and responsibilities outside the EU for performing the *in vivo* skin irritation study on the substance subject to this decision, questioning the requirement to provide the Annex VII standard information. Regarding the latter, it was already explained above why the assessment of the information generated at Annex VII level needs to be considered and documented. Moreover, ECHA notes that no supporting evidence was provided regarding the general statements of global responsibilities outside of the EU.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to provide the assessment performed for the skin irritation endpoint (i.e. the standard information requirement as specified in Annex VII, 8.1), on which basis you decided to perform an *in vivo* skin irritation study in accordance with Annex VIII, section 8.1.

2. The assessment performed for the eye irritation endpoint (standard information requirement as specified in Annex VII, 8.2.) on the registered substance on which basis an *in vivo* eye irritation study was performed in accordance with Annex VIII, section 8.2.

According to Article 41(1)(a) of the REACH Regulation ECHA may verify whether the information submitted by registrants was generated in compliance with the requirements of Articles 10, 12 and 13 of the REACH Regulation and with Annexes III and VI to X.

Pursuant to Article 13(1) of the REACH Regulation in particular information on human toxicity shall be generated whenever possible by means other than vertebrate animal tests, through the use of alternative methods, for example *in vitro* methods.

The introductory note to Annex VI provides that "*the precise information requirements will differ, according to tonnage, use and exposure, and the requirements of the corresponding Annex have to be considered in addition to the prior Annexes. The Annexes shall thus be considered as a whole, and in conjunction with the overall requirements of registration, evaluation and the duty of care*". Furthermore, as specified in the first paragraph of the introductory note of Annex VIII the information required under column 1 of Annex VIII is additional to that required in column 1 of Annex VII. Moreover, according to the third paragraph of that note before new tests are carried out all available information (including *in vitro* data) shall be assessed first.

With a view to eye irritation, according to Annex VII, 8.2 to the REACH Regulation, the assessment of the endpoint shall comprise, consecutively, an assessment of the available human and animal data, an assessment of the acid or alkaline reserve, and an *in vitro* study for eye irritation.

According to the Annex VIII, section 8.2., an *in vivo* eye irritation study is a standard information requirement. ECHA's Guidance on information requirements and chemical safety assessment further provides that for substances registered at above 10 tonnes the *in vivo* study for eye irritation should be provided, in case the information requirement cannot be met with the information obtained as specified in section 8.2 of Annex VII. (See guidance R.7a, chapter R.7.2.7.2 (July 2015)). In particular, the guidance states as follows:

> *"Before new tests are carried out to determine the properties listed in Annex VIII, all available in vitro data, in vivo data, historical human data, data from valid (Q)SARs and data from structurally related substances (read-across approach) must be assessed first. Due to the sequential nature of the REACH standard information requirements, it is reminded that at quantities of >10 tpa, the information requirements of Annex VII to the REACH Regulation also apply. This means that before a new in vivo test is performed, the appropriate in vitro testing must be undertaken according to the rules set out in section 8.2 of Annex VII and must be documented in the technical dossier (IUCLID). Finally, the information generated at Annex VII level must be taken into account in determining whether an in vivo test at Annex VIII level is really needed".*

ECHA notes that you have provided an *in vivo* eye irritation study according to EU method B.5/OECD 405 performed between 11 and 21 July 2011 in order to fulfil the information requirement for Annex VIII, section 8.2.

However, the registration dossier does not document the information that should have been generated in accordance with Annex VII, section 8.2. Furthermore, the registration dossier does not show how information required under Annex VII, section 8.2 was taken into account in determining the need for the *in vivo* test. Accordingly, the relevant assessment required under Annex VII, section 8.2 is missing in the registration dossier and therefore does not enable ECHA to determine you have complied with the requirement in Article 13(1) of the REACH Regulation to generate information whenever possible by means other than vertebrate testing.

In your comments to the draft decision, you did not provide any further information on the assessment of information in accordance with Annex VII, section 8.2, but instead indicated regulatory requirements and responsibilities outside the EU for performing the *in vivo* eye irritation study on the substance subject to this decision, questioning the requirement to provide the Annex VII standard information. Regarding the latter, it was already explained above why the assessment of the information generated at Annex VII level needs to be considered and documented. Moreover, ECHA notes that no supporting evidence was provided regarding the general statements of global responsibilities outside of the EU.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to provide the assessment performed for the eye irritation endpoint (standard information requirement as specified in Annex VII, 8.2), on which basis you decided to perform an *in vivo* eye irritation study in accordance with Annex VIII, section 8.2.

3. Justification for performing, on the registered substance, the Guinea Pig Maximisation Test (EU method B.6/OECD 406) instead of the Local Lymph Node Assay (EU method B.42/OECD 429), as specified in Annex VII, 8.3, column 2

According to Article 41(1)(b) of the REACH Regulation ECHA may verify whether the adaptations of the standard information requirements and the related justifications submitted in the submitted dossier comply with the rules governing such adaptations.

Annex VII, section 8.3, column 2 to the REACH Regulation states that *'[t]he Murine Local Lymph Node Assay (LLNA) is the first-choice method for in vivo testing. Only in exceptional circumstances should another test be used. Justification for the use of another test shall be provided.'*

ECHA notes that you have provided a Guinea Pig Maximisation Test (GPMT) according to EU method B.6 (OECD 406) in the dossier to fulfil the aforementioned REACH information requirement for skin sensitisation. The study was performed between 7 July and 12 August 2011.

No justification has been provided in the registration dossier why this study has been conducted instead of the LLNA. The LLNA specified in the REACH Regulation is a refinement and reduction method that causes less suffering to the animals and requires reduced number of animals in comparison to the guinea pig test method specified in the EU method B.6 (OECD 406).

In your comments to the draft decision, you indicated that the lack of justification for performing the GMPT was an oversight and that the dossier will be updated to include this after the decision has been issued. ECHA welcomes this statement and invites you to update the registration accordingly to bring it into compliance with the REACH requirements. ECHA also reminds you that the justification to be provided needs to be substance specific and adequately documented.

Therefore, you are requested to provide adequate justification for the performance of the GPMT (EU method B.6/OECD 406) instead of the Local Lymph Node Assay (EU method B.42/OECD 429).

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 4 September 2015.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation:

ECHA notified you of the draft decision and invited you to provide comments. ECHA took into account your comments, which were sent within the commenting period, and they are reflected in the Reasons (Appendix 1).
ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment.

ECHA received a proposal for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment.

ECHA referred the draft decision to the Member State Committee.

You did not provide any comments on the proposed amendment.

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-47 meeting and ECHA took the decision according to Article 51(6) 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 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 your Member State.