ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-2114303733-58-01/F Helsinki, 4 September 2015

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

For sodium thiocyanate, CAS No 540-72-7 (EC No 208-754-4), 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 thiocyanate, CAS No 540-72-7 (EC No 208-754-4), submitted by [redacted] (Registrant). The scope of this compliance check decision is limited to the standard information requirements of Annex VI, Section 2 and Annex VIII, Sections 8.1.1. and 8.2.1 of the REACH Regulation.

This decision is based on the registration as submitted with submission number [redacted], for the tonnage band of 1000 tonnes or more tonnes 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 22 October 2013.

On 28 November 2013 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision. That draft decision was based on submission number [redacted].

On 9 January 2014 ECHA received comments from the Registrant.

On 7 March 2014 2014 the Registrant updated his registration dossier (submission number , [redacted]).

The ECHA Secretariat considered the Registrant's comments and the update. On basis of this information, Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

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, proposals for amendment to the draft decision were 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 proposals 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 , in accordance to Article 51(5), the Registrant provided comments on the proposals for amendment. The Member State Committee took the comments of the Registrant on the proposals for amendment into account.

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

A. Information in the technical dossier derived from the application of Annexes VII to XI

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

In vivo eye irritation (Annex VIII, 8.2.1.; test method: OECD 405 as updated 2 October 2012);

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 **12 September 2016**.

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 sound 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 in this decision, or to fulfil otherwise the information requirement with a valid and documented adaptation, will result in a notification to the Authorities of the Member States for possible enforcement.

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.

A. Information in the technical dossier derived from the application of Annexes VII to XI

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 X of the REACH Regulation.

In vivo eye irritation

"*In vivo* eye irritation" is a standard information requirement as laid down in Annex VIII, Section 8.2.1. 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.
The Registrant has sought to adapt this information requirement pursuant to column 2 of Annex VIII, Section 8.2.1. The justification of the adaptation given by the Registrant is: "*In the BCOP the IVIS is 49 which is just below the threshold for severe irritancy/corrosion of 55.1. Therefore the test substance is not regarded to cause irreversible effects to the eye but on the other hand also not a non-irritant. Consequently performing an in vivo test is scientifically unjustified and the substance can best be classified as Irritating to eyes (Category 2).*"

The study referred in the waiver is an OECD guideline 437 "Bovine corneal opacity and permeability (BCOP) test method with the registered substance for identifying ocular corrosives and severe irritants". However, despite the highest reliability assigned in the dossier by the Registrant to this study, several important elements are missing from the reporting in the dossier, including the following: how many eyes have been used for each group and the reporting of those results, what was the post-exposure period, what where the negative and positive control results (only stated that within the historical control ranges). Moreover, test conditions were not properly specified, there were missing individual data on test samples i.e. opacity and OD490 values for the test substance, data from replicates are also missing.

Furthermore, while this test is recommended for use as part of a tiered-testing strategy for regulatory classification and labelling within a specific applicability domain, it is not considered valid as a complete replacement for the *in vivo* rabbit eye test.

The BCOP study provides insufficient information and also is not capable to give in fact any clear indications if the substance is a category 2 eye irritant. One of the identified limitations of this test method is the high false negative rate for solids observed in validation database (even though the substance was tested in 20% solution as advised in the testing guideline). Furthermore, after 240 minutes of treatment with Sodium thiocyanate the mean *in vitro* irritancy score (IVIS) was 49 and because it was below the threshold (55.1) it was considered by the Registrant not to be severely irritant or corrosive in this test system. However, these values are quite close and given the identified poor suitability for solids of this test method, testing with a method more appropriate for solids should be performed.

ECHA notes that the possibilities of adaptation for this requirement as defined in Column 2, of Annex VIII, Section 8.2.1 require that:
"- the substance is classified as irritating to eyes with risk of serious damage, or
-the substance is classified as corrosive to the skin and provided that the registrant classified the substance as eye irritant, or
-the substance is a strong acid (pH less than 2) or base (pH more than 11.5), or
-the substance is flammable in air at room temperature".

In section 2.1. of the IUCLID dossier the Registrant classified the substance as Eye Irrit.2 (H319: Causes serious eye irritation). However, the risk of serious eye damage, as listed as adaptation in the above mentioned column 2 of Annex VIII, implies a classification as Eye Irrit 1 (H318: Causes serious eye damage), not a category 2. In addition, the substance is not classified as corrosive to the skin. Finally, the substance is neither strong acid nor base and is not flammable at room temperature.

Therefore, the adaptation of the information requirement suggested by the Registrant could not be accepted.

During the commenting period on draft decision the Registrant argued against the decision:"
All the arguments by ECHA are formally correct. However, from an animal ethical point of view we have a difficulty to perform an in vivo eye irritation study with a substance that is shown in the BCOP test to be almost reaching the classification border for serious eye damage."

For eye irritation endpoint, in the updated dossier the Registrant has included additional *in vitro* (BCOP) and *in vivo* read-across data from ammonium thiocyanate (NH4SCN) to support their conclusion on the classification for the eye irritation potential for this registered substance i.e. sodium thiocyanate.

In its read-across argumentation the Registrant states the following *"Additional data is available from cross-reading to Ammonium thiocyanate (NH4SCN).*
An older in vivo study in rabbits performed on the pure NH4SCN substance only showed mild irritation. However, as no observation after 72hr were performed to demonstrate recovery, an additional in vitro BCOP study was performed to aid in the interpretation of the results. This study resulted to a very high IVIS score of 120, clearly pointing to severe eye damage.

Comparing the results from the BCOP study on NH4SCN with that of the in vivo study in rabbits, the BCOP seems to possibly over-predict the effects for Ammonium thiocyanate. In the disseminated dossier on Ammonium chloride (CAS 12125-02-9) the key study on eye irritation involves an in vivo rabbit study. For results it was reported as irritating, with full reversibility within 1 week. The severe effects of NH4SCN in the BCOP test are therefore not considered to be solely related to the ammonium cation, and the over prediction of the BCOP test is likely to be at least partly caused by the thiocyanate anion. "

The Registrant proposes the following adaptation to avoid performing the in vivo eye irritation study "*The BCOP test on NaSCN resulted to an IVIS of 49. This score very close to the threshold of 55. Therefore, although the threshold is set at a level favouring false positive compared to false negatives, there is still a possible concern that these results for NaSCN lead to a false negative classification for serious eye damage; i.e. should be classified as Cat.1 eye damage after all. However, information from studies on NH4SCN give indication that the BCOP test possibly over predicts effects of thiocyanate.*

Lack of skin irritation as well as profiling for eye irritation in QSAT Toolbox (v3.2) supports the low risk for severe eye irritation. As classification as eye irritant can be sufficiently decided upon based on available data, no further in vivo studies are needed to confirm the classification as eye irritant cat.2."

However, ECHA notes the following several flaws in the argumentation provided by the Registrant.

The Registrant states that BCOP seems to overpredict the effects of NH4SCN based on the contradicting results obtained in the BCOP (category 1) and an old *in vivo* assay (category 2). However, in the category justification document the Registrant proposes that NH4SCN should be classified as Cat 1 eye damage and this has been also included in the dossier of NH4SCN submitted by the same Registrant. With this statement, the Registrant is contradicting with their statement that BCOP seems to overpredict the hazard of thiocyanates, since based on the information submitted it seems that they consider the result of the BCOP assay to be more accurate than the results from the *in vivo* assay. In addition, the read-across between NaSCN and NH4SCN is questionable. ECHA notes that the Registrant himself stated in his category justification document available in the dossier, for local effects, that the ammonium ion is not representative for the Na salt. ECHA considers that the ammonium ion has distinct properties from Na+ ions, and that the consequences of this difference are not taken into account. Accordingly, ECHA considers that the proposed read-across from the ammonium thiocyanate does not enable that the human health effects of the registered substance may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach). Additionally, for in vivo eye irritation, the requirement of Annex XI, 1.5, that if the group concept is applied, substances shall be classified and labelled on this basis, is not met, since the classification of ammonium thiocyanate is not applied for the registered substance by the Registrant. Thus the adaptation using ammonium thiocyanate fails to meet the requirements of Annex XI, 1.5 and cannot be accepted.

In their comments, the Registrant explains further how he follows the ITS (Integrated testing strategy) for eye irritation as presented in the ECHA Guidance R.7.a. This approach has some flaws e.g. by stating *"Here the BCOP test indicated with the agreed threshold of 55.1 that the substance is NOT R41. So we should consider R36 – which we did. But even when continuing through the scheme and come to the part on new testing, already 8a gives the same results:*

Does the substance demonstrate irritating or non-irritating properties in validated in vitro or ex vivo tests (adopted by OECD or not) for eye irritation?
YES: the substance clearly indicates irritating properties in view of the high IVIS score 49. If YES: Classify accordingly (R36, R41 or no classification) ***. If discrimination between R41 and R36 is not possible, R41 must be chosen. So we classify R36, as the IVIS score was below the agreed threshold of 55.1 for classification."*** The conclusions of the Registrant are not according to the ITS presented in ECHA Guidance R.7a and not according to the BCOP test guideline. The test guideline OECD 437 describes in paragraph 6 (as does the Registrant in his comments) that *"Moreover, BCOP false negatives in this context are not critical since all test chemicals that produce an 3 < IVIS ≤ 55 would be subsequently tested with other adequately validated in vitro tests, or as a last option in rabbits, depending on regulatory requirements, using a sequential testing strategy in a weight-of-evidence approach."* Therefore the Registrant's approach to choose the classification as category 2 eye irritant does not follow the recommendations on how to interprete the results of the BCOP test, since based on the results obtained from the NaSCN (IVIS 49)

further testing should be performed in order to conclude on the hazard properties of the substance. The reason behind is that, based on the IVIS score 49, it is not possible to conclude if the substance should merit a classification of category 1 or category 2 (based on the information provided by the dossier, it seems that the substance is hazardous for the eyes, but the severity of these effects cannot be confirmed based on the data provided by the Registrant).

Therefore, based on the information provided, the conclusion of the Registrant to classify the substance as category 2 eye irritant based on BCOP assay does not cover fully the information requirement for the *in vivo* eye irritation as specified in the Annex VIII, section 8.2.1, REACH, since the result obtained from the study does not allow to conclude on the hazardous properties of the registered substance.

The Registrant provided in the comments also information from grouping, profiling and QSARs on the substances NaSCN, KSCN and NH4SCN. ECHA has taken the information provided into account and concludes that the weight-of-evidence approach is not sufficient to conclude whether the substance is a severe, moderate or not irritant and that therefore the standard information requirement for this endpoint could not be adapted.

As explained above, the information available 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.

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: Acute eye irritation/corrosion (test method: OECD 405 as updated 2 October 2012).

IV. Adequate identification of the composition of the tested material

ECHA stresses that the information submitted by 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

In relation to the information required by the present decision, the sample of substance used for the new study 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 study 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 study 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 study 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://echa.europa.eu/appeals/app_procedure_en.asp. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

Authorised[1] by Ofelia Bercaru, 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.