ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 13 December 2018

Addressee
[redacted]

Decision number
CCH-D-2114453558-39-01/F

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: N-acetylsulphanilyl chloride
EC number: 204-485-1
CAS number: 121-60-8

Your registration
Registration number: [redacted]
Submission number: [redacted]
Submission date: 10 February 2015
Registered tonnage band: 10-100 (tonnage band submission [redacted])

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA requests you to submit information generated with a test material representative of the Substance on:

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

2. **Screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: OECD TG 421 or 422 in rats, oral route;**

You are required to submit the requested information in an updated registration dossier by ***20 April 2020***.

You are required to submit the results in a form of a robust study summary[1]. You shall also update the chemical safety report.

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.

The scope of this compliance check decision is limited to the standard toxicological information requirements of Annex VIII, to the REACH Regulation.

[1] See ECHA Practical guide 3: https://echa.europa.eu/documents/10162/13643/pg_report_robust_study_summaries_en.pdf/

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[2] by Ofelia Bercaru, Head of Unit, Evaluation E3

[2] 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

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

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

For your registration an In vitro gene mutation study in mammalian cells is a standard information requirement if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained. ECHA notes that the registration dossier contains negative results for both these information requirements. Therefore, adequate information on in vitro gene mutation in mammalian cells needs to be present in the technical dossier for the Substance to meet this information requirement.

You have not provided any information for this endpoint and therefore, there is a data gap that needs to be filled.

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.

In your comments to the draft decision you indicated that this study is not a standard information requirement for registrations at 10-100 tonnes per year. As explained above, an *in vitro* gene mutation study in mammalian cells is a standard information requirement if negative results were obtained in the *in vitro* gene mutation in bacteria assay and in an *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study conducted according to the information requirements of Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2, respectively. Since your dossier reports negative results from these *in vitro* studies, an *in vitro* gene mutation study in mammalian cells is a standard information requirement.

Also, you indicate that "*since there is already data available for the substance which confirms that the substance not genetically toxic substance*". This statement is not scientifically justified based on the available information in the currrent registration dossier. Adequate information on in vitro gene mutation in mammalian cells needs to be present in the technical dossier for the Substance to meet this information requirement.

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

For your registration a "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 Substance to meet this information requirement.

You provided the following information for "Toxicity to Reproduction":

1. An automated report generated with the OECD QSAR Toolbox indicating that is used to predict LOEL for the Substance based on read-across; and
2. A Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (OECD TG 422) performed with a proposed analogue substance (4-methylbenzenesulfonyl chloride EC No: 98-59-9 / CAS No:202-684-8).

You have further provided a document entitled "category justification" that contains categorisation/read-across apporach for the Substance (the target substance) with the use of the functionalities by the QSAR Toolbox and other modeling software. You have identified Tosyl chloride (CAS No: 98-59-9) as an analogue substance (the source substance) for use of read-across on the basis of common functional groups identified by the modelling software. You summarised the experimental study for the source substance as well as the automated generated prediction for the target substance with the OECD QSAR Toolbox mentioned above to support the hypothesis for similar toxicity.

ECHA notes that:

1. You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance for the information provided within the OECD QSAR Toolbox report;
2. You have not provided an assessment to address structural similarity/dissimilarity between the target and the source substances for the prediction / read-across proposal as presented within the automated OECD QSAR Toolbox reports;
3. You have not provided an assessment to address structural dissimilarity between the target and th source substances for the read-across proposal as presented in the category justification document. The target substance contains an additional acetylamino group compared to the source substance; and
4. You have not provided experimental studies neither with the target substance nor with structurally similar source substance(s) which would substantiate the prediction for the information requirement of a reproductive toxicity study. Absence of relevant experimental data to substantiate the hypothesis for the prediction makes any adaptation based on read-across invalid as it does not allow a comparative assessment of properties of the source and target substance and hence concluding whether properties could be read across.

You have further indicated in the Technical Dossier that you consider the information you provided in the Endpoint Study Records for "Toxicity to reproduction" for in a Weight of Evidence Approach.

ECHA notes that the information provided as explained above, does not constitute relevant and reliable information in the context of a weight of evidence approach.

ECHA therefore concludes that:

- The proposed adaptation is not in line neither with the conditions specified in Annex XI, Section 1.5., nor with those specified in Annex XI, Section 1.2.,and is therefore rejected.
- Contrary to Article 3(28) of the REACH Regulation, the documentation of the endpoint study records is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment.

According to the test method 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 solid ECHA concludes that testing should be performed by the oral route.

In your comment on a proposal for amendment submitted by a Member State Competent Authority, you have claimed that the substance has only intermediate use and that you had further changed the tonnage band of your registration from 10-100 tonnes per year to 1-10 tonnes per year. Therefore you consider that the screening study for reproductive/developmental toxicity should be removed from the decision. Without addressing the merit of your claim (which is not supported by data) ECHA notes that there are other registrant(s) in the joint submission who remain at Annex VIII level. Also, as outlined in Appendix 2 of this decision, updates of the registration dossier after the notification of the draft decision are not to be considered. Exceptionally, your initial change of the tonnage from Annex IX to Annex VIII information requirements was already taken into account. Further/later changes and updates cannot be considered in the current decision making process.

Deadline to submit the requested information in this decision

In the draft decision communicated to you the time indicated to provide the requested information was 24 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also requested a Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.) and a Pre-natal developmental toxicity study (Annex IX, Section 8.7.2). Due to the tonnage band change from 100-1000 tonnes per year to 10-100 tonnes per year, these two requests have been removed from the present decision. Following a proposal for amendment from one of the Member States Competent Authorities the request for a Screening study for reproductive/developmental toxicity (OECD TG 421/422) was included in the decision. Hence, ECHA considers that a reasonable time period for providing the required information in the form of an updated registration is 16 months from the date of the adoption of the decision. The decision was therefore modified accordingly.

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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. Exceptionally, following your comments on the draft decision indicating a tonnage band downgrade, ECHA has taken into account the updated tonnage band in submission number [redacted] submission date 09 August 2018, only. No assessment of the updated registration dossiers has occurred. Based on the average production and/or import volumes for the three preceding calendar years, ECHA has changed the tonnage band as basis for the draft decision from 100 - 1000 tonnes per year (submission number: [redacted] (submission date 10 February 2015)) to 10 - 100 tonnes per year (submission number: [redacted]).

The compliance check was initiated on 16 January 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 your information about a tonnage band downgrade.

This has resulted in the removal of the following decision requests: Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats, and Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route.

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

ECHA received proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments.

ECHA referred the draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

In addition, you provided comments on the draft decision. These comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5).

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-62 written procedure 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 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 relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported 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 the substance tested in the new tests is appropriate to assess the properties of the Substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally 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.