EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002399-65-05/F Helsinki, 23 April 2013

**DECISION ON A TESTING PROPOSAL SET OUT IN A REGISTRATION PURSUANT TO ARTICLE 40(3) OF REGULATION (EC) NO 1907/2006**

**For N-Butylbenzenesulphonamide, CAS No 3622-84-2 (EC No 222-823-6), 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 40(1) of the REACH Regulation, ECHA has examined the following testing proposals submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12(1)(e) thereof for N-Butylbenzenesulphonamide, CAS No 3622-84-2 (EC No 222-823-6), by [redacted] (Registrant).

- Stability in organic solvents and identity of relevant degradation products;
- Dissociation constant study according to OECD Guideline 112;
- Viscosity study according to OECD Guideline 114;
- Developmental toxicity/teratogenicity study according to OECD Guideline 414;
- Biodegradation in water according to OECD Guideline 309;
- Biodegradation in soil according to OECD Guideline 307.

This decision is based on the registration dossier as submitted with submission number [redacted], for the tonnage band of 1000 or more per year. This decision does not take into account any updates after 14 June 2012, the date upon which ECHA notified its draft decision to the Compentent Authorities of the Member States pursuant to Article 51(1) of the REACH Regulation.

This decision does not imply that the information provided by the Registrant in his registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA to initiate a compliance check on the present dossier at a later stage.

On 01 October 2010, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of the testing proposals set out by the Registrant in the registration dossier for the substance mentioned above.

ECHA held a third party consultation for the testing proposals from 14 February 2011 until 31 March 2011. ECHA did receive information from third parties (see section III below).

On 23 March 2012 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

By 23 April 2012 the Registrant did not provide any comments on the draft decision to ECHA.

On 14 June 2012 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 to amend the draft decision within 30 days of the receipt of the notification.

Subsequently, Competent Authorities of the Member States submitted proposals for amendment to the draft decision.

On 18 July 2012 ECHA notified the Registrant of proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on those proposals for amendment within 30 days of the receipt of the notification.

ECHA has reviewed the proposals for amendment received and decided to amend the draft decision.

On 30 July 2012 ECHA referred the draft decision to the Member State Committee.

The Registrant did not provide any comments on the proposed amendments.

A unanimous agreement of the Member State Committee on the draft decision was reached on 3 September 2012 in a written procedure launched on 22 August 2012 and ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Testing required

The Registrant shall carry out the following proposed tests pursuant to Article 40(3)(a) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

1. Stability in organic solvents and identity of the relevant degradation products study; Annex IX, 7.15.
2. Dissociation constant in water study; Annex IX, 7.16.; test method: OECD 112.
3. Viscosity study (viscosity in liquids), Annex IX, 7.17.; test method: OECD 114.
4. Pre-natal developmental toxicity study in rats, oral route (Annex IX, 8.7.2.; test method: EU B.31/OECD 414).
5. Biodegradation in water study (aerobic mineralisation in surface water – simulation biodegradation test); Annex IX, 9.2.1.2.; test method: EU C.25/OECD 309.
6. Biodegradation in soil study (aerobic and anaerobic transformation in soil); Annex IX, 9.2.1.3.; test method: EU C.23/OECD 307.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **23 October 2014** an update of the registration dossier containing the information required by this decision.

Before conducting any of the tests mentioned above in points 5 and 6 the Registrant is advised to consult the ECHA *Guidance on information requirements and chemical safety assessment (version 3.0, November* 2012), Chapter R7b, Sections R.7.9.4. and R.7.9.6. and Chapter R.11.1.3. on PBT assessment to determine the sequence in which the simulation tests are to be conducted and the necessity to conduct the second simulation test.

Data from a second pre-natal developmental toxicity study on another species is a standard information requirement according to Annex X, 8.7.2. of the REACH Regulation. 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. 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.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposals submitted by the Registrant for the registered substance and scientific information submitted by third parties.

**1. Stability in organic solvents and identity of relevant degradation products**

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test. Stability in organic solvents and identification of relevant degradation products study is a standard information requirement as laid down in Annex IX, section 7.15. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to generate the data for this endpoint. The Registrant shall use a test method that is suitable to generate appropriate data for the registered substance subject to the present decision.

**2. Dissociation constant**

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test. Dissociation constant is a standard information requirement as laid down in Annex IX, section 7.16. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to generate the data for this endpoint.

**3. Viscosity**

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test. Viscosity study is a standard information requirement as laid down in Annex IX, section 7.17. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to generate the data for this endpoint.

**4. Pre-natal developmental toxicity**

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test. 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. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to generate the data for this endpoint.

The Registrant did not specify the species and route to be used for testing. 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 as a first species to be used.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation. For the reasons explained further below the information provided by third parties is not sufficient to fulfil this information requirement.

Third party information 1:

Before a pre-natal developmental toxicity study (OECD Guideline 414) is conducted, consideration should be given to the following alternative testing strategies:

1. Evaluate the need to conduct a pre-natal developmental toxicity study (OECD Guideline 414) in light of the results of the existing Reproduction/Developmental Toxicity Screening Test (OECD Guideline 421) and other toxicological data.
2. Perform in vitro (pre-) validated tests for the evaluation of the embryotoxic and endocrine disruption potential and apply QSAR classification models for developmental toxicity. Use results to waive developmental toxicity study (Prenatal Developmental Toxicity Study, OECD Guideline 414).
3. Exposure considerations: use the TCC for reproduction toxicity endpoint.

In addition to these alternative testing strategies a prediction from the CAESAR model has been provided.

ECHA examined the comments and concluded the following:

The third party has proposed three testing strategies (1, 2, 3, as referred above) for ECHA to consider before further tests on animals are requested. However, third parties were invited, as specified by Article 40(2) of the REACH Regulation to submit "scientifically valid information and studies that address the relevant substance and hazard end-point, addressed by the testing proposal". As the proposal for a strategy as such cannot be regarded information or studies, ECHA concludes that this is not a sufficient basis to fulfil the data/information requirement.

The third party has also proposed the result from the QSAR classification model for developmental toxicity. The result from the QSAR classification model is not suitable for the purposes of classification and labelling and/or risk assessment for the endpoint for which the testing has been proposed to meet the information requirement (Annex IX, 8.7.2.). The documentation provided is inadequate and it has not been shown if the scientific validity of the model has been established or not. Therefore, the conditions specified in Annex XI, 1.3 are not met and the results cannot be used instead of testing. The submitted documents also indicate that the substance might be outside of the applicability domain of the model.

Therefore, ECHA concludes that the information submitted does not meet the conditions for the adaptation on the basis of QSAR models set out in Annex IX, Section 1.3. Therefore, it cannot constitute an acceptable adaptation to standard information requirements.

Third party information 2:

The third party has proposed to use a result of the QSAR model called Nonlinear classification ANN QSAR Model for prenatal developmental toxicity study.

The result from the QSAR classification model (i.e. "toxic" / "non-toxic") is not suitable for the purposes of classification and labelling and/or risk assessment for the endpoint for which testing has been proposed to meet the information requirement (Annex IX, 8.7.2.). Compliance with the Annex XI section 1.3 requirements could not be established as the required information concerning the validity, adequacy for classification and labelling and documentation of the model was not provided. The (Q)SAR Model Reporting Format (QMRF) does not provide sufficient information to deduce whether the training set was constructed from studies that cover the information requirements of the OECD 414 guideline, or important study aspects, such as the species, dose selection and number of animals used. In addition, the submitted QMRF does not contain any indication on the adequacy in relation to a defined regulatory purpose of the Testing Proposal.

Therefore, ECHA concludes that the information submitted does not meet the conditions for the adaptation on the basis of QSAR models set out in Annex XI, Section 1.3. Therefore, it cannot constitute an acceptable adaptation to standard information requirements.

c) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Pre-natal developmental toxicity study in rats, oral route (test method: EU B.31/OECD 414) using the registered substance.

When considering the need for a testing proposal for a prenatal developmental toxicity study in a second species, the Registrant should take into account the outcome of the pre-natal developmental toxicity study on the first species and all 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.

At any time, the Registrant shall take into account that there may be an obligation to make every effort to agree on sharing of information and costs with other Registrants.

**5. and 6. Simulation testing (biodegradation in surface water and soil)**

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

According to column 1 of Section 9.2.1.2 and 9.2.1.3 of Annex IX of the REACH Regulation, simulation testing on ultimate degradation in surface water and soil simulation testing are standard information requirements. The information on these endpoints are not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there are information gaps and it is necessary to provide information for data for these endpoints.

The Registrant has submitted a testing proposal for simulation biodegradation study in surface water (EU C.25/OECD 309) and a testing proposal for an aerobic and anaerobic transformation in soil simulation biodegradation study (EU C.23/OECD 307) to cover these endpoints. In the technical dossier, the Registrant provided no justification for conducting the proposed tests. However, ECHA notes that the proposed tests can be used to fulfil the information requirements for simulation testing on ultimate degradation in surface water and for soil simulation testing.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed studies: Aerobic mineralisation in surface water – simulation biodegradation test (Annex IX, 9.2.1.2.; test method: EU C.25/OECD 309) using the registered substance and Aerobic and anaerobic transformation in soil – simulation biodegradation test (Annex IX, 9.2.1.3.; test method: EU C.23/OECD 307) using the registered substance.

In addition, ECHA considers that based on the information available in the technical dossier, (18% degradation after 28 days using OECD 301B test method), the substance is potentially meeting the P or the vP criterion. As the assessment of the vP criterion as per Annex XIII can be based on one simulation test, it is advisable that one simulation test shall be performed first. The impact on the CSA, of the results of first simulation test and, if appropriate, other required tests shall be evaluated before proceeding with the required second simulation test.

The order in which the simulations tests are performed, needs to take into account the intrinsic properties of the registered substance and the identified use and release patterns which could significantly influence the environmental fate of the substance. The Registrant is advised to consult the REACH guidance on information requirements chemical safety assessment Chapter R.11.1.3. and Figure R. 11-1 on PBT assessment for the integrated testing strategy for persistency assessment.

Furthermore, ECHA would advise the Registrant to consider the following notes of concern on degradation testing and uncertainity of the water solubility of the registered substance:

- In the technical dossier, there is one biotic degradation test. There is no other biotic degradation tests for example enhanced readily biodegradation test. The results from such studies would not, by themselves, fulfil the information requirement of Annex IX section 9.2.1.2. and 9.2.1.3., but may provide the basis for adaptation of the standard information requirements provided by the REACH Regulation.

- There is remaining uncertainty in the water solubility value used for the registered substance and its effect on other instrinisic properties, in particular, Log Kow as a number of tests are waived due to the Log Kow value of 2.01.

IV. General requirements for the generation of information and Good Laboratory Practice

ECHA always reminds registrants of the requirements of Article 13(4) of the REACH Regulation that ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP).

According to Article 13(3) of the REACH Regulation, tests that are required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the European Chemicals Agency as being appropriate. Thus, the Registrant shall refer to Commission Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 as adapted to technical progress or to other international test methods recognised as being appropriate and use the applicable test methods to generate the information on the endpoints indicated above.

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 appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on the 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.

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