EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-0000005230-88-02/F Helsinki, 2 October 2014

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

For betaine, CAS No 107-43-7 (EC No 203-490-6), 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 41(1) of the REACH Regulation ECHA has performed a compliance check of the registration for betaine, CAS No 107-43-7 (EC No 203-490-6, submitted by [redacted] (Registrant). The scope of this compliance check is limited to the standard information requirement of Annex VIII, Section 8.4.3. of the REACH Regulation. ECHA stresses that it has not checked the information provided by the Registrant 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 12 June 2014, 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 13 May 2013.

On 24 July 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 August 2013 ECHA received comments from the Registrant on the draft decision.

The ECHA Secretariat considered the Registrant's comments and update.

The information is reflected in the Statement of Reasons (Section III) whereas no amendments to the Information Required (Section II) were made.

On 12 June 2014 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.

As no proposals for amendment were submitted, ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

II. Information required

Pursuant to Articles 41(1), 41(3), 10(a)(vii), 12(1)(e), 13 and Annex VIII 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:

- In vitro gene mutation study in mammalian cells (Annex VIII, 8.4.3.; test method: EU B.17/OECD 476).

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 **9 October 2015**.

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. The scope of the present decision is the *in vitro* gene mutation study in mammalian cells (Annex VIII, 8.4.3. of the REACH Regulation).

Mutagenicity, *in vitro* gene mutation study in mammalian cells.

In accordance with Articles 10(a)(vii), 12(1)(e) and with Annex VIII, section 8.4.3. of the REACH Regulation, the *in vitro* gene mutation study in mammalian cells is required if there is a negative result in the *in vitro* studies specified under Annex VII, section 8.4.1 and Annex VIII, section 8.4.2. The registration dossier reports negative results for both *in vitro* studies. Therefore the REACH Regulation requires that information on *in vitro* gene mutation in mammalian cells (Annex VIII, 8.4.3.) is provided in the dossier. ECHA notes furthermore that a cytogenicity study (be it *in vitro* or *in vivo*) cannot be used for *in vitro* or *in vivo* mammalian cell gene mutation information requirements. Cytogenicity studies and gene mutation studies are corresponding to two different endpoints and two distinct mechanisms of genotoxicity: cytogenicity studies detect structural and numerical chromosome aberrations whereas gene mutation studies detect gene or point mutations. ECHA concludes that the Registrant has neither provided this standard information nor adapted the requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

The Registrant submitted comments and updated the dossier with a justification for adapting the information requirement for the in vitro study in mammalian cells included in IUCLID Section 7.6.1. In this adaptation the Registrant refers to a combined 52-week

chronic and 104-week carcinogenicity test in rats (OECD 453, Combined Chronic Toxicity / Carcinogenicity Studies), for which the results are summarised in section 7.7. of the IUCLID dossier. There were no neoplastic histopathological findings reported in the study. This, in the Registrant opinion, shows that there are no concerns for carcinogenicity and that the dossier also demonstrates that betaine does not exhibit any properties that would indicate a reproductive or teratogenic concern.

ECHA points out that REACH Annex VIII section 8.4.3 column 2 does not provide a possibility to use carcinogenicity study results, negative or positive, to adapt the information requirement for a gene mutation study in mammalian cells. Moreover, lack of carcinogenicity in a single study is not sufficient evidence that the substance is not mutagenic. Although a mutagenic substance would normally be assumed to be carcinogenic, it cannot be assumed that all mutagens are necessarily detected in a cancer bioassay. Furthermore, mutagenicity can have implications not only for cancer but also for possible transfer of mutations to offspring. The dossier does not contain a study for reproductive or developmental toxicity (teratogenicity). A Combined Chronic Toxicity / Carcinogenicity Study cannot be used to draw conclusions on these endpoints.

Therefore, pursuant to Article 41(1)(a) 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: *In vitro* mammalian cell gene mutation test (test method: EU B.17./OECD 476).

IV. Adequate identification of the composition of the tested material

ECHA stresses that the information submitted 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 to ensure that his registration covers one substance only and that the substance is correctly identified in accordance with Annex VI, Section 2 of the REACH Regulation.

In carrying out the study required by the present decision it is important to ensure that the particular sample of substance tested 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. If the registration of the substance covers different grades, the sample used for the new study must be suitable to assess these.

Furthermore, 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.

Leena Ylä-Mononen
Director of Evaluation