ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002631-81-04/F Helsinki, 31/10/2012

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

For Slimes and Sludges, blast furnace and steelmaking, CAS No 65996-73-8 (EC No 266-006-2), 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 jointly submitted registration dossier in accordance with Articles 10(a)(ix) and 12(1)(e) thereof for Slimes and Sludges, blast furnace and steelmaking, CAS No 65996-73-8 (EC No 266-006-2), by [redacted] (Registrant) to fulfil the information requirements set out in Annex IX:

- Genetic toxicity *in vivo*, Mammalian Erythrocyte Micronucleus Test (OECD 474).

This decision is based on the registration dossier 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 after 19 July 2012, 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.

In accordance with Articles 10(a)(ix) and 12(1)(d) of the REACH Regulation, the Registrant submitted the following testing proposal as part of the registration dossier.

On 11 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 15 September 2011 until 31 October 2011. ECHA received information from third parties (see section III below).

On 12 April 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. The draft decision referred to has a submission number [redacted].

On 14 May 2012 the Registrant provided to ECHA comments on the draft decision and on 7 June 2012 the Registrant updated his registration dossier (submission number [redacted]) removing two of the three previously submitted testing proposals (i.e., proposals for a developmental toxicity / teratogenicity study and for two-generation reproductive toxicity study).

ECHA considered the Registrant's comments received and the dossier update and amended Sections II and III accordingly.

On 19 July 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 22 August 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 reviewed the proposals for amendment received and decided to amend the draft decision.

On 3 September 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 8 October 2012 in a written procedure launched on 26 September 2012 and ECHA took the decision pursuant to Article 51(6) 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 requirements of the REACH Regulation. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

II. Testing required

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

- *In vivo* Mammalian erythrocyte micronucleus test (Annex IX, 8.4, column 2; test method: EU B.12/OECD 474).

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **31 October 2013** an update of the registration dossier containing the information required by this decision.

If the result of the Mammalian erythrocyte micronucleus test is negative, the Registrant should consider performing an *in vivo* gene mutation test and submit a corresponding testing proposal to ECHA.

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.

III. Statement of reasons

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

***In vivo* Mammalian erythrocyte micronucleus test**

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.

Pursuant to Annex IX, section 8.4, column 2, if there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and there are no results from an *in vivo* study available, an appropriate *in vivo* somatic cell genotoxicity test shall be proposed by the Registrant. The Registrant reported the following three *in vitro* mutagenicity studies:

- Mutagenicity - Reverse Mutation Test Using Bacteria (EU Method B.13/14). The study was negative with and without metabolic activation;
- *In vitro* Mammalian Chromosome aberration Test (OECD 473). The first experiment was negative with and without metabolic activation and the second experiment was negative without metabolic activation and positive with metabolic activation providing an overall equivocal result;
- *In vitro* Mammalian cell gene mutation test (OECD 476). The Registrant reports "biologically relevant increases of mutants" after treatment, with and without metabolic activation, and the effect showed a dose-response. The dossier indicates that there was also an increase in small colonies with metabolic activation, which would indicate a clastogenic effect. The result is positive.

The Registrant justifies the testing proposal as follows: "By reason that one of the tests had positive results, it is not possible to exclude genetic toxicity of the test substance. For confirmation this possibility will be proved In Vivo Mammalian Erythrocyte Micronucleus Test (OECD Guideline 474)."

During the Registrant's commenting period, the Registrant provided a general comment to the draft decision. Following the comment the dossier was updated and two out of three testing proposals were withdrawn and therefore, the comment became irrelevant to the current decision.

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 below the information provided by third parties is not sufficient to fulfil this information requirement.

A third party proposes to omit the test for *in vivo* genotoxicity because none of the components of the substance are known to be genotoxic *in vivo* and many of them are essential elements. In addition, the third party states that positive results obtained in the *in vitro* studies are not considered to be relevant to the situation *in vivo* because of predicted low systemic absorption and normal cellular defences.

The third party has proposed a strategy 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.

c) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: *In vivo* Mammalian erythrocyte micronucleus test (Annex IX, 8.4, column 2; test method: EU B.12) using the registered substance.

Based on the provided *in vitro* genotoxicity studies, a genotoxic effect by gene mutational mechanism cannot be excluded. More specifically, the study summary of the *in vitro* Mammalian Cell Gene Mutation Test (EU B.17/OECD 476) does not indicate clearly that the positive result is caused by an increase in small colonies only, i.e. indicating mainly or exclusively a clastogenic mechanism. Therefore, if the result of the Mammalian erythrocyte micronucleus test is negative, the Registrant is recommended to consider performing an *in vivo* gene mutation test. If the Registrant considers it necessary to perform an *in vivo* gene mutation test, he should send a testing proposal to ECHA along with the updated dossier.

IV. Adequate identification of the composition of the tested material

The process of examination of testing proposals set out in Article 40 of the REACH Regulation aims at ensuring that the new study meets real information needs. Within this context, the Registrant's dossier was sufficient to confirm the identity of the substance to the extent necessary for examination of the testing proposal. The Registrant must note, however, that this information, or the information submitted by other registrants of the same 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 proposed test, 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 of the same substance to agree to the test proposed (as applicable to their tonnage level) 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 grades registered to enable the relevance of the study to be assessed.

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

ECHA 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). National authorities monitoring GLP maintain lists of test facilities indicating the relevant areas of expertise of each facility.

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.

VI. 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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Director of Regulatory Affairs