~~CONFIDENTIAL~~

European Chemicals Agency

Decision number: CCH-D-0000001717-70-07/F Helsinki, 12 December 2011

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

For 2,2'-(Ethylenedioxy)diethanol, CAS No. 112-27-6 (EC No. 203-953-2); 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 41(1) of the REACH Regulation the ECHA has performed a compliance check of the registration dossier for **2,2'-(Ethylenedioxy)diethanol, CAS No. 112-27-6 (EC No. 203-953-2)**, submitted by [redacted] (Registrant), latest submission number [redacted], for 1000 tonnes or more per year.

The compliance check was initiated on 9 July 2010.

On 8 June 2011 ECHA notified the Registrant of its draft decision and invited him pursuant to Article 50(1) of the REACH Regulation to provide comments within 30 days of the receipt of the draft decision.

The Registrant submitted comments on the draft decision on 1 July 2011. ECHA considered the Registrant's comments received and did not amend the draft decision.

On 29 July 2011 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. Subsequently, Competent Authorities of the Member States submitted proposals for amendment to the draft decision.

On 31 August 2011 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 within 30 days of the receipt of the notification.

The Registrant did not provide comments on the proposals for amendment.

ECHA reviewed the proposals for amendments received and decided to modify the draft decision accordingly.

On 12 September 2011 ECHA referred the draft decision to the Member State Committee.

A unanimous agreement of the Member State Committee on the modified draft decision was reached on 14 October 2011 in a written procedure launched on 3 October 2011.

This compliance check decision does not prevent ECHA to initiate further compliance checks on the present dossier at a later stage.

II. Information required

1) Pursuant to Articles 41(1)(a), 41(3) and 10(a)(ii) as well as Annex VI, section 2 of the REACH Regulation the Registrant shall submit for the registered substance:

    a. The composition of the substance (Annex VI, 2.3.),
    b. Gas chromatogram (Annex VI, 2.3.6.).

2) Pursuant to Articles 41(1)(a), 41(3), 10(a)(vii), 12(1)(e), 13 and Annex VIII of the REACH Regulation the Registrant shall submit the information using the test method as indicated on:

    a. Mutagenicity: *in vitro* gene mutation study in mammalian cells (Annex VIII, 8.4.3.; EU Method B.17.),
    b. Mutagenicity: *in vitro* gene mutation study in bacteria with an additional, fifth strain of bacteria (Annex VII, 8.4.1) following an updated recommendations of EU Method B.13/14 (OECD Test Guideline 471).

Pursuant to Article 41(4) of the REACH Regulation the Registrant shall submit the information in the form of an updated IUCLID dossier to ECHA by 13 September 2012 – 9 months from the date of the decision.

III. Statement of reasons

Based on the examination of the technical dossier, ECHA concludes that the information therein, submitted by the Registrant for registration of the above mentioned substance for the purpose of registration within the applicable tonnage band of 1000 tonnes or more per year in accordance with Articles 6 of the REACH Regulation, does not comply with the requirements of Articles 10, 12 and 13 and with Annexes VI and VIII thereof. Consequently, the Registrant is requested to submit the information mentioned above that is needed to bring the registration into compliance with the relevant information requirements.

The Registrant expressed consent to ECHA's initial draft decision when providing comments on it and did not take a position on the proposal to require an *in vitro* gene mutation study in bacteria with an additional fifth strain (see point 2(b) below)

1) Missing information related to substance identity

Pursuant to Article 10(a)(ii) and Annex VI, section 2 of the REACH Regulation, the technical dossier of the registration shall include information on the identity of the substance. Annex VI, section 2 lists information requirements that shall be sufficient to identify the registered substance.

(a) The composition of the substance (Annex VI, 2.3.)

The purity of the substance as given in the technical registration dossier is not consistent with the specified concentration ranges for the main constituent and impurities. The minimum purity is ca. [redacted] while the sum of all the listed impurity maximum concentrations is less than [redacted] Therefore, [redacted] of the substance composition is unaccounted for based on the information provided in the dossier. The Registrant is requested to provide a degree of purity as required by Annex VI, 2.3.1. of the REACH Regulation that is consistent with the specified impurity concentration ranges.

(b) Gas chromatogram (Annex VI, 2.3.)

The registration contains a gas chromatogram of the registered substance. However, the chromatogram does not enable the composition of the substance to be quantified. None of the impurities listed in section 1.2 can be identified or quantified based on the submitted data. Therefore the Registrant is requested to provide a chromatogram that includes information on the identity and concentrations of the substance's impurities. The chromatogram shall be consistent with the information on the composition of the substance, as described in section 1.2 of the technical dossier.

2) Missing information related to endpoints

Pursuant to Articles 10(a)(vii) and 12(1)(e) of the REACH Regulation, a registration for a substance produced in quantities of 1000 tonnes or more per year shall contain as a minimum the information specified in Annexes VII-X of the REACH Regulation.

(a) Mutagenicity: *in vitro* gene mutation study in mammalian cells (Annex VIII, 8.4.3.; EU Method B.17.):

The technical dossier contains the results of an *in vitro* gene mutation study in bacteria, showing negative results, an *in vitro* mammalian chromosome aberration test, showing negative results, and an *in vitro* sister chromatid exchange assay in mammalian cells, also showing negative results. Annex VIII, 8.4.3. requires information on *in vitro* gene mutation study in mammalian cells, if a negative result is obtained in the tests in *in vitro* gene mutation study in bacteria and the *in vitro* cytogenicity study. This information is not included in the technical dossier, and no justification is provided for omitting this information.

Therefore, the Registrant is requested to submit the information for this endpoint performed with the registered substance.

(b) Mutagenicity: *in vitro* gene mutation study in bacteria with an additional, fifth strain of bacteria (Annex VII, 8.4.1) following an updated recommendations of EU Method B.13/14 (OECD Test Guideline 471)

ECHA notes that for the endpoint 8.4.1 of Annex VII, the Registrant provided data from an *in vitro* gene mutation study in bacteria performed in *Salmonella typhimurium* according to OECD Test Guideline (TG) 471 in force at that time and in accordance with the OECD good laboratory practice (GLP) principles.

According to Article 13(3) of the REACH Regulation, tests required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods recognised by the Commission or ECHA. Other tests may be used if the conditions of Annex XI are met.

In the present case, the test submitted was carried out according to GLP and to OECD TG 471. However, since the test was conducted, significant changes have been made to OECD 471 and this means that the study does not meet the current guidelines, nor can it be considered as providing equivalent data according to the criteria in Annex XI.

The version of the EU Test Method B.13/14/OECD TG 471 in force since 1997 introduces the need for performing the test in at least 5 strains of bacteria whereas the OECD TG 471 in force in 1986 only required testing in a minimum of 4 bacterial strains. The required 5th bacterial strain, i.e. *Escherichia coli WP2* strains or *S. typhimurium TA102*, has the potential to detect certain types of mutagens, such as cross-linking agents or oxidising mutagens, which the 4 bacterial strains recommended in the former version of the OECD TG 471 may not detect.

Consequently, the Registrant is required to complete the data set on mutagenicity by performing an *in vitro* gene mutation study in bacteria (Annex VII, 8.4.1), on the registered substance, using one missing bacterial strain which may detect mutagens, such as cross-linking agents or oxidising mutagens, i.e. one *E. coli WP2* strain or *S. typhimurium TA102*, following recommendations of EU Method B.13/14 laid down in Commission Regulation (EC) No 440/2008 or OECD Test Guideline 471.

IV. <u>General requirements for the generation of information and Good Laboratory Practice</u>

ECHA always reminds registrants of the requirements of Article 13(4) of the REACH Regulation that reads:

> "Ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice provided for in Directive 2004/10/EC or other international standards recognised as being equivalent by the Commission or the Agency and with the provisions of Directive 86/609/EEC, if applicable."

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 and use the applicable test methods to generate the information on the endpoints indicated above.

National authorities monitoring good laboratory practice (GLP) maintain lists of test facilities indicating the relevant areas of expertise of each facility.

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.

Done at Helsinki,

[redacted]

Jukka Malm
Director of Regulatory Affairs