EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-0000002339-71-07/F Helsinki, 15 June 2012

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

For 2,2'-ethylenedioxyethyl bis(2-ethylhexanoate), CAS No 94-28-0 (EC No 202-319-2), 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'-ethylenedioxyethyl bis(2-ethylhexanoate), CAS No 94-28-0 (EC No 202-319-2), submitted by [redacted] (Registrant), latest submission number [redacted], for 1000 tonnes or more per year.

The compliance check was initiated on 28 April 2011.

On 9 August 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.

On 7 September 2011 the Registrant provided to ECHA comments on the draft decision. Both on 6 September 2011 and 8 December 2011 dossier updates were received.

ECHA has taken into account the information received and decided to amend the draft decision.

On 2 March 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, one Competent Authority of a Member State submitted a proposal for amendment to the draft decision.

On 4 April 2012 ECHA notified the Registrant of the proposal for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on that proposal for amendment within 30 days of the receipt of the notification.

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

On 16 April 2012 ECHA referred the draft decision to the Member State Committee.

On 27 April 2012 the Registrant provided comments on the proposed amendment. The Member State Committee took the comments of the Registrant into account.

A unanimous agreement of the Member State Committee on the draft decision was reached on 21 May 2012 in a written procedure launched on 10 May 2012.

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

II. Information required

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

> Pre-natal developmental toxicity study in the rat via the oral route (Annex IX, 8.7.2.; test method: EU B.31/ OECD 414).

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 16 June 2014**. 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

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 above 1000 tonnes per year in accordance with Articles 6 and 11(2) of the REACH Regulation, does not comply with the requirements of Articles 10, 12 and 13 and with Annex IX, 8.7.2. 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 initial draft decision sent to the Registrant on 9 August 2011 also contained the request for a two-generation reproductive toxicity study (Annexes IX/X section 8.7.3.) and for a pre-natal developmental toxicity study (Annex X section 8.7.2.) for a second species. ECHA notes that there is an ongoing discussion at EU level in relation to the standard information requirement for a two-generation reproductive toxicity study and has decided not to address this standard information requirement in the current compliance check. Furthermore, as the pre-natal developmental toxicity study for a second species was part of the tiered testing strategy proposed by the Registrant in his comments to the original draft decision, ECHA has decided to also not address the standard information requirement of a second pre-natal developmental toxicity study in the current compliance check. The requests for these two endpoints were, therefore, removed from the draft decision.

1. Missing information related to endpoints

Pursuant to Articles 41(1)(a) and (b), 41(3), 10(a)(vii), 12(1)(e), 13 and Annex IX 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 to X of the REACH Regulation.

- Pre-natal developmental toxicity study (Annex IX, 8.7.2.)

The technical dossier contained adaptations to the standard information requirement for the endpoint on pre-natal developmental toxicity study (Annex IX, 8.7.2.). The Registrant includes a waiving argument stating that *'the study does not need to be performed unless the 90 day sub-chronic toxicity study indicates otherwise'*. Furthermore *'based upon Annex XI, substance-tailored exposure-driven waiving is proposed. Testing in accordance with Sections 8.6 and 8.7 (repeated dose and reproductive toxicity testing) of Annex VIII, IX and X may be omitted, based on the exposure considerations. The use of substance in* [redacted] *does not result in significant exposure (incorporated in a matrix), however the use in* [redacted] *could result in measurable exposure to professionals and consumers. Additional support for waiving this test are the (a) the lack of reproductive toxicity effects in the 28-day/reproductive OECD 422 toxicity screening study with the substance and (b) the relevance of the dermal exposure route which would result in low systemic exposure. Moreover, according to REACH Art. 13(1) and 25(1) states that if the generation of information by means other than tests may be possible, the use of vertebrate animals in testing should be undertaken only as a last resort'.*

However, the specific rules for adaptation from the information requirements set out in the second column of section 8.7. of Annex IX REACH provide that the reproductive toxicity studies do not need to be conducted if:

- the substance is known to be a genotoxic carcinogen and appropriate risk management measures are implemented, or
- the substance is known to be a germ cell mutagen and appropriate risk management measures are implemented, or
- the substance is of low toxicological activity, no systematic absorption occurs and there is no significant human exposure.

The first two conditions are not fulfilled. The third condition is also not fulfilled as the 28-day study showed toxicological activity (effects in the thymous, spleen, thyroid gland, pituitary, whilst there was a decreased proportion of neutrophils in the highest group of females tested). Furthermore, as the substance is not classified, there is no exposure assessment for the registered substance that would indicate no exposure.

In response to ECHA's draft decision, the Registrant updated the registration dossier on 6 September 2011 and 8 December 2011 with Annex XI, section 3.2(a) adaptations to omit testing for pre-natal developmental toxicity in the rat. Furthermore, the Registrant argued that the two-generation reproductive toxicity study and the second pre-natal developmental study that were contained in ECHA's initial draft decision would be dependent on the results of the first pre-natal developmental study and the sub-chronic repeated dose toxicity study (90 day). The sub-chronic repeated dose toxicity study was proposed by the Registrant and is subject to a testing proposal examination that is performed by ECHA in parallel to the present compliance check.

With regards to the exposure based adaptation, ECHA notes that sufficient evidence needs to be provided for the absence or no significant exposure in all exposure scenarios of the manufacture and all identified uses. This has not been shown in the dossier update. In order to meet the conditions for exposure based adaptation as laid down in Annex XI, 3.2(a) of the REACH Regulation. The Registrant did not explain and document the levels of dermal exposure compared to the related derived no effect level (DNEL), as well as inhalation exposure concentrations for exposure scenario 3 compared to the DNEL for inhalation. In all cases, discrepancies in the assessment factors used compared to the ones indicated in the Guidance on *Information Requirements and Chemical Safety Assessment* (R.8, version 2, December 2010) needs to be fully justified.

In conclusion, as conditions for exposure based adaptation are not met, the registration dossier is not in compliance for the endpoint of Annex IX, 8.7.2, the Registrant is accordingly requested to submit the information performed with the registered substance subject to the present decision for a pre-natal developmental toxicity study in the rat via the oral route (Annex IX, 8.7.2.; EU Method B.31 or OECD 414).

2. Period of time for conducting the test

As stated above the Registrant submitted a testing proposal for the sub-chronic toxicity endpoint (Annex IX, 8.6.2.). The decision on the testing proposal is communicated to the Registrant in a separate decision.

In the initial draft decision communicated to the Registrant on 9 August 2011, the time indicated to provide the requested information was 36 months from the date of adoption of the decision. This period of time took into account the fact that the initial draft decision also requested a two-generation reproductive toxicity study and a pre-natal developmental toxicity study in a second species. As it was decided not to address in this draft decision any potential deficiencies with respect to the compliance of the dossier with the standard information requirements set out in Annex X, 8.7.2. and 8.7.3., ECHA considers that a reasonable time period for providing the remaining required information in the form of an updated IUCLID5 dossier is 24 months from the date of the adoption of the decision. The maximum period of 24 months is also taking into account the time needed to perform the sub-chronic toxicity study addressed in the testing proposal examination decision. The decision was therefore modified accordingly.

IV. Adequate identification of the composition of the tested material

ECHA stresses that the information submitted by other joint Registrants 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.

In relation to the information required by the present decision, 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 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 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 grade 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).

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 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.

[redacted]

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Director of Regulatory Affairs