ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002255-79-03/F Helsinki, 25/07/2012

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

For Acetalization products between glucose and C16/18(even numbered)- alcohol (List No 927-870-2), 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 testing proposals set out in the registration dossier for Acetalization products between glucose and C16/18(even numbered)- alcohol (List No 927-870-2) submitted by [redacted] (Registrant).

This decision is based on the registration dossier as submitted with submission number [redacted], for 100 - 1000 tonnes per year. This decision does not take into account any updates submitted after 2 March 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.

In accordance with Articles 10(a)(ix) and 12(1)(d) of the REACH Regulation, the Registrant submitted the following testing proposals as part of the registration dossier to fulfil the information requirements set out in Annex IX:

- Further information on adsorption/desorption according to OECD test guideline 106 (Adsorption – Desorption Using a Batch Equilibrium Method);
- Sub-chronic toxicity study (90-day) according to OECD test guideline 408 (Repeated Dose 90-day Oral Toxicity in Rodents); and
- Short-term toxicity to invertebrates according to OECD test guideline 207 (Earthworm, Acute Toxicity Tests).

On 8 April 2009, 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 opened a third party consultation for the testing proposals including testing on vertebrate animals that was held from 15 September 2011 until 31 October 2011 and received information from third parties (see Section III below).

On 4 January 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 3 February 2012 the Registrant did not provide any comments on the draft decision to ECHA.

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, Competent Authorities of the Member States did not propose amendments to the draft decision and ECHA took the decision pursuant to Article 51(3) 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 to initiate a compliance check on the present dossier at a later stage.

II. Testing required

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

1. Further information on adsorption/desorption (Annex IX, 9.3.3., test method EU C.18/OECD 106).

Pursuant to Article 40(3)(b) of the REACH Regulation, the Registrant shall carry out the following test under modified conditions using the indicated test method and the substance subject to the present decision:

2. Sub-chronic toxicity study (90-day), (Annex IX, 8.6.2., Repeated dose toxicity, test method: B.26/OECD 408) in rat by the oral route. The study protocol shall be modified with additional clinical pathology and histopathological evaluations to evaluate effects on male reproductive organs as described in OECD 416, paragraphs 29-32, 39, 41-44.

Pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant shall carry out either of the following tests using the indicated test method and the substance subject to the present decision:

3. Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*), (Annex IX, 9.4. column 2, Long-term toxicity to invertebrates, test method: OECD 222)
   or,
   Earthworm, acute toxicity test (Annex IX, 9.4.1., Short-term toxicity to invertebrates, test method: EU C.8/OECD 207).

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA **by 27 January 2014** an update of the registration dossier containing the information required by this decision.

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 of the Registrant for the registered substance and scientific information submitted by third parties.

1. Further information on adsorption/desorption

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

Further information on adsorption/desorption is a standard information requirement as laid down in Annex IX, section 9.3.3. 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.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study Further information on adsorption/desorption (test method: EU C.18/OECD 106) using the registered substance.

2. Sub-chronic toxicity study (90-day)

a) Examination of the testing proposal

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

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, section 8.6.2. 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 short-term repeated dose toxicity study (28-day) carried out with the registered substance revealed multiple, statistically significant effects on sperm parameters. While the Registrant concluded that these effects are not chemically-related, ECHA considers that these parameters should be investigated further in the proposed 90-day study. A chemically-related effect could thereby be clarified and either excluded or confirmed. The measurement of sperm parameters is not an obligatory part of the B.26 (sub-chronic toxicity study, 90-day) test method. However, paragraph 1.5.2.3 of the test method provides that one may "need to examine additional tissues" which is necessary to conclude on the described effects in the lower tier study. Suitable methods of how to investigate the effects on sperm can be found in OECD test guideline 416 paragraphs 29-32, 39, 41-44.

The Registrant proposed testing by the oral route. In the light of the physico-chemical properties of the substance and the information provided on the uses and human exposure, ECHA considers that testing by the oral route is appropriate. The Registrant did not specify the species to be tested. According to the test method EU B.26/OECD 408 the rat is the preferred rodent species. ECHA considers this species as being appropriate.

Therefore, pursuant to Article 40(3)(b) of the REACH Regulation, the Registrant is required to carry out the proposed study under modified conditions: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD 408) using the registered substance. The study protocol shall be modified with additional clinical pathology and histopathological evaluations to evaluate effects on male reproductive organs; specifically as described in OECD 416, paragraphs 29-32, 39, 41-44.

b) Consideration of the third party information

ECHA received third party information concerning the testing proposal during the public 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.

The third party has proposed not to conduct the proposed OECD 408 study for acetalization products between glucose and C16-18(even numbered)-alcohol but supplement the registration dossiers by repeated doses toxicity data of C12/16 alkyl polyglycosides as key study for the repeated dose toxicity endpoint. Such a subchronic study in rats is cited in a toxicological text book (Handbook of Detergents, CRC Press, 2004) and in a notification to US FDA (2007).

According to section 1.5. of Annex XI of the REACH Regulation, grouping of substances and read-across approach can be applied for substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity, and when the conditions in section 1.5. of Annex XI are met.

The substances included in the category built by the Registrant and the substance proposed for read across by the third party are all UVCB substances (Substances of Unknown or Variable composition, Complex reaction products or Biological materials). The information provided does not allow ECHA to conclude that the conditions of section 1.5. Annex XI of the REACH Regulation are met. ECHA acknowledges that the Registrant may himself supplement under its own responsibility the argumentation and information provided by the third party in order to make use of adaptation possibilities. This would require that the Registrant demonstrates a sufficient justification to build a category or to use read-across, according to the criteria laid down in Annex XI of the REACH Regulation.

Third party information 2.

A third party proposed an in vitro dermal study strategy for ECHA to consider before further tests on animals are requested.

However, third parties were invited, as specified by Article 40(2) 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 for rejecting the Testing Proposals.

3. Long-term toxicity testing on invertebrates

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

Toxicity to terrestrial organisms and in particular on invertebrates is a standard information requirement as laid down in Annex IX, section 9.4.1. of the REACH Regulation. Column 1 of Annex IX, 9.4.1. of REACH specifies a short-term test as the standard information requirement. However, column 2 of that Annex specifies that long-term toxicity testing shall be considered by the registrant instead of short-term if the substance has a high potential to adsorb to soil. As the registered substance is highly adsorptive, long-term tests should be preferred as the condition of column 2 is met. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to

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meet the information requirements. Consequently there is an information gap and it is necessary to generate the data for this endpoint.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is given a choice between carrying out the preferred (long-term) earthworm reproduction test (OECD 222) or – if long-term testing is not considered being appropriate – to perform a (short-term) earthworm acute toxicity test (test method EU C.8/OECD 207) instead. Any of the two tests should be performed using the registered substance subject to this decision.

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 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 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.

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 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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