EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002595-69-03/F Helsinki, 24.09.2012

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

For di(morpholin-4-yl) disulphide, CAS No 103-34-4 (EC No 203-103-0), 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 proposal submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12 (1)(d) thereof for di(morpholin-4-yl) disulphide, CAS No 103-34-4 (EC No 203-103-0), by [redacted] (Registrant).

- 90-day oral toxicity study (OECD 408), no indication of the substance to be tested given;

This decision is based on the registration dossier as submitted with submission number [redacted] for the tonnage band of 100 to 1000 tonnes 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.

This decision does not imply that the information provided by the Registrant in his registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the present dossier at a later stage.

On 23 November 2010, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated an examination of three 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 29 April 2011 until 14 June 2011. ECHA did not receive information from third parties.

On 25 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.

On 16 May 2012 ECHA received comments from the Registrant agreeing to ECHA's draft decision. Also, as indicated in the comments, on the same day the Registrant updated his registration dossier and removed two of the three testing proposals initially present, i.e. testing proposals for long-term toxicity testing on fish and on invertebrates.

ECHA considered the Registrant's comments received and did amend the draft decision.

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 did not propose amendments to the draft decision and ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

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.

II. Testing required

The Registrant shall carry out the following additional test pursuant to Article 40(3)(c) of the REACH Regulation using the indicated test methods and the registered substance:

1. Sub-chronic toxicity study (90-day) in rats, inhalation route (Annex IX, 8.6.2., test method: EU B.29/OECD 413).

while the originally proposed test for a Sub-chronic toxicity study (90-day) in rats, oral route (Annex IX, 8.6.2., test method: EU B.26/OECD 408 proposed to be carried out using the registered substance is rejected pursuant to Article 40(3)(d) of the REACH Regulation.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **24 March 2014** an update of the registration dossier containing the information required by this decision.

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.

1. Repeated dose toxicity

Pursuant to Article 40(3)(d) of the REACH Regulation ECHA may reject the proposed test.

Pursuant to Article 40(3)(c) of the REACH Regulation, ECHA may require the Registrant to carry out additional tests in case of non-compliance of the testing proposal with Annexes IX, X or XI of the REACH Regulation.

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 Registrant proposed testing by the oral route, but the selection of the route for the Testing Proposal was not justified. In the light of the physico-chemical properties of the substance and the information provided on the uses and human exposure, ECHA considers that the oral route is not the most appropriate route, but testing should be performed via the inhalation route.

According to REACH, Annex IX, Column 2 "Specific rules for adaptation from Column 1", testing by the inhalation route is appropriate if "*exposure to humans via inhalation is likely taking into account the vapour pressure of the substance and/or the possibility of exposure to aerosols, particles or droplets of an inhalable size*".

ECHA considered whether the inhalation route is appropriate. Although the particle size distribution of the substance indicates that the majority of the particles will be filtered out before they reach the lungs, there is a proportion of the particles (6%) with diameter below 10 microns; this portion is of an inhalable size. In addition, in the Exposure Scenarios and the Risk Characterization sections in the CSR, the Registrant has identified inhalation as one of the routes of exposure. Thus the information above shows that the inhalation route is appropriate for the test on the substance. Furthermore, there is a concern that the substance is more potent by the inhalation route than the oral route. The NOAEL via inhalation is 9.8 mg/m3 air in the 28-day study, i.e. approximately ~3 mg/kg/day; whereas by the oral route the NOAEL is 250 mg/kg/day in the prenatal developmental toxicity study. For these reasons, ECHA is of the opinion that inhalation is the most appropriate route for testing.

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is required to carry out the following study: Sub-chronic toxicity study (90-day) in rats, inhalation route (test method: EU B.29/OECD 413) using the registered substance, whereas the originally proposed test has been rejected in accordance with Article 40(3)(d).

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.

IV. Adequate identification of the composition of the tested material

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. 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.

Furthermore, 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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Jukka Malm
Director of Regulatory Affairs