ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-0000001475-74-03/F Helsinki, 11 July 2012

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

For 2-benzyl-2-dimethylamino-4'-morpholinobutyrophenone, CAS No [redacted] (EC No 404-360-3); 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, ECHA has performed a compliance check of the registration dossier for substance 2-benzyl-2-dimethylamino-4'-morpholinobutyrophenone, CAS No [redacted] (EC No 404-360-3), submitted by [redacted] (Registrant), latest submission number [redacted], for 1 - 10 tonnes per year.

The compliance check was initiated on 30 September 2010.

On 4 January 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 12 January 2011 the Registrant provided to ECHA comments on the draft decision. ECHA amended the draft decision accordingly.

On 4 November 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 did not propose amendments to the draft decision and ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

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), 41(3), 10(a)(vi), 12(1)(a) and 13 as well as Annex VII of the REACH Regulation, the Registrant shall submit the following information using the test method as indicated below:

- *In vitro* gene mutation study in bacteria (Annex VII, 8.4.1) using one 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.

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 **11 July 2013.**

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 in accordance with **Article 6** of the REACH Regulation, does not comply with the requirements of Articles **10, 12 and 13 and Annex VII** 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.

Missing information related to Mutagenicity

Pursuant to Articles 10(a)(vi), 12(1)(a) and (b) of the REACH Regulation, a registration for a substance manufactured or imported in quantities of 1-10 tonnes per year shall contain as a minimum the information specified in Annex VII of the REACH Regulation.

ECHA notes that for the endpoint 8.4.1 of Annex VII, *in vitro* gene mutation study in bacteria, the Registrant provided data from an *in vitro* gene mutation study in bacteria performed in 1991, according to OECD Test Guideline (TG) 471 in force at that time and in accordance with the OECD good laboratory practice (GLP) principles. This data was provided to the Registrant by ECHA pursuant to Article 25(3) of the REACH Regulation as a response to the inquiry submitted by the Registrant pursuant to Article 26 of the REACH Regulation.

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. According to Commission Regulation (EC) No 440/2008 lying down tests methods, the *in vitro* gene mutation study in bacteria should be performed in accordance with the current OECD TG 471. This 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 1991 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.

Annex XI, 1.1.2 of the REACH Regulation details the conditions under which data obtained from experiments not carried out according to GLP or to the test methods referred to in Article 13(3) of the REACH Regulation shall be considered to be equivalent to data generated by the corresponding test methods referred to in Article 13(3).

ECHA considers that the *in vitro* gene mutation study in bacteria submitted by the Registrant differs from the test protocol detailed in the EU Test Method B. 13/14 OECD TG 471 because the battery of bacterial strains used to perform this test does lack one strain with the capacity to detect certain types of mutagens, such as cross-linking agents or oxidising mutagens. The data set submitted does not provide an adequate and reliable

coverage of the key parameters foreseen to be investigated in the EU Test Method B. 13/14 OECD TG 471 and therefore does not meet the condition laid down in Annex XI, 1.1.2 (2) of the REACH Regulation.

During the commenting period, the Registrant indicated that the information which is currently in the dossier on endpoint 8.4.1. (*in vitro* gene mutation study in bacteria) was provided to him by ECHA during the inquiry process (as the data was already available to ECHA and it was submitted at least 12 years previously). The Registrant further claims that if such data does not meet the information requirement under REACH it should not had been provided by ECHA. In the response to the Registrant's comment ECHA notes that it does not endorse the quality of the data submitted under previous legislation and that it is the Registrant's responsibility to assess the quality of the data provided to him during the inquiry process before deciding on its adequacy for the registration purposes.

Additionally, the Registrant proposed to fulfil the information requirement for endpoint 8.4.1. *in vitro* gene mutation in bacteria (Annex VII), with alternative test data, either the *in vitro* cytogenicity study in mammalian cells (endpoint 8.4.2., Annex VIII) or the *in vitro* gene mutation study in mammalian cells (endpoint 8.4.3., Annex VIII or IX). However, ECHA notes that these studies, proposed as alternative by the Registrant, are related to other information requirements and they do not cover the standard information requirement of Annex VII, 8.4.1. of the REACH Regulation.

Consequently, the Registrant is required to complete the data set on mutagenicity by performing an *in vitro* gene mutation test in bacteria by using one additional 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 updated recommendations of EU Method B. 13/14 or OECD TG 471.

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 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.

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.

[redacted]

Geert DANCET
Executive Director