~~CONFIDENTIAL~~

European Chemicals Agency

Decision number: TPE-D-0000001704-77-03/F Helsinki, 28/09/2011

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

For 5-METHYLHEXAN-2-ONE, CAS NO 110-12-3 (EC NO 203-737-8), 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 (the REACH Regulation).

I. Procedure

Pursuant to Article 40(1) of the REACH Regulation, ECHA has examined a testing proposal set out in the registration dossier for **5-methylhexan-2-one, CAS No 110-12-3 (EC NO 203-737-8)**, submitted by [redacted] (the "Registrant"), latest submission number [redacted], for above 1000 tonnes per year.

In accordance with Article 12(1)(e) of the REACH Regulation, the Registrant submitted the following testing proposal as part of the registration dossier to fulfil the information requirements set out in Annexes IX and X:

- Developmental toxicity in rats, OECD Guideline 414.

The examination of the testing proposal was initiated on 6 September 2010.

ECHA opened a third party consultation for the testing proposal including testing on vertebrate animals that was held from 14 February 2011 until 31 March 2011. ECHA received comments from third parties concerning in vitro testing, the use of TTC concept, the read-across from other substances, inclusion of the substance in the regulatory programmes of non-European authorities and QSAR models (see Section III and the attached documents on third party information).

On 7 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.

By 7 July 2011 the Registrant did not provide any comments on the draft decision to ECHA.

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 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 tests:

- Pre-natal developmental toxicity test in rats, oral route (Annex IX, 8.7.2, method B.31 of Regulation (EC) No 440/2008; OECD test guideline 414).

A decision on the need to perform another pre-natal developmental study on a second species shall be based on the outcome of the first developmental study and all other relevant available data (REACH Annex X, 8.7.2).

Pursuant to Article 40(4) and 22 of the REACH Regulation, the Registrant shall submit the information listed above in the form of an updated IUCLID dossier to ECHA by 28 September 2012 - 12 months from the date of the decision. In this dossier update the Registrant shall make a proposal on another pre-natal developmental study on a second species, if considered necessary based on performed studies and all other relevant data.

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.

Developmental toxicity test

ECHA has examined the scientific information submitted by the third parties, as follows:

Third party information 1: The third party has proposed four types of information for ECHA to consider, i.e. the use of in vitro testing, the use of TTC concept, read-across from other substances, and unspecified data in other regulatory programmes of non-European authorities. Considering that ECHA invited submission of "scientifically valid information and studies that address the relevant substance and hazard end-point, addressed by the testing proposal", as specified by Article 40(2), ECHA has evaluated the information provided by the third party. ECHA has concluded that the proposed

information does not sufficiently address the relevant endpoint. Consequently, ECHA concludes that the information provided is not a basis for rejecting the testing proposed.

Third party information 2: A prediction using the nonlinear classification ANN QSAR Model for prenatal developmental toxicity study giving the result toxic was provided. The dependent variable of the model is in the form "toxic/non-toxic". Annex XI, 1.3 governing QSAR models requires that information concerning the validity, applicability domain, adequacy for classification & labelling, and documentation of the method be provided. As this information was not provided, ECHA considers that the model fails to meet the requirements of Annex XI, 1.3. The predicted result can therefore not be directly used or extrapolated to fill the information requirements in question.

ECHA agrees with the Registrant that a pre-natal developmental toxicity test is needed to address the information requirements of Annexes IX and X, 8.7.2 of the REACH Regulation. Since the information for developmental toxicity in one species is required by both Annexes IX and X and the requirements are additive, the information requirements from these two Annexes comprise pre-natal developmental toxicity tests in two species. However, according to column 2 of Annex IX, 8.7.2, the decision on the need for performing the test in a second species should be based on the outcome of the study in the first species and all other relevant data.

Once the information from the first study is available, and taking into account all relevant information, the Registrant is requested to consider whether the information requirements for pre-natal developmental toxicity studies in two species are met and update his dossier accordingly. The updated dossier shall either include an explanation, why the Registrant considers the information requirements as being met, or a testing proposal for a pre-natal developmental toxicity study in a second species, preferably in rabbit.

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 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.

Done at Helsinki,

Jukka Malm
Director of Regulatory Affairs