~~CONFIDENTIAL~~

European Chemicals Agency

Decision number: CCH-D-0000001474-76-03/F Helsinki, 14 April 2011

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

For [redacted], 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 41(1) of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (the REACH Regulation), ECHA has performed a compliance check of the registration dossier for [redacted] (the "Registrant"), latest submission number [redacted], for 1 - 10 tonnes per year.

The compliance check was initiated on 16 August 2010.

The draft decision was sent to the Registrant for comments on 5 January 2011.

On 2 February 2011 the Registrant sent a comment stating that he has no objections to the draft decision sent by ECHA.

On 18 February 2011, ECHA notified the Member State Competent Authorities of its draft decision and invited them to propose amendments and to comment on the draft decision.

By 21 March 2011, ECHA did not receive any proposals for amendments from the Competent Authorities of the Member States.

European Chemicals Agency
Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland
Tel.: +358 9 6861 80 | Fax +358 9 6861 8210 | http://echa.europa.eu

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

II. Information required

A) Pursuant to Articles 41(1)(a), 41(3), 10(a)(vi), 12(1)(a), and Annex VII of the REACH Regulation, the Registrant shall submit the missing elements to complete the study summaries as defined by Article 3(29) on the following endpoints:

- Melting/freezing point (Annex VII, 7.2.)
  i. Type of method used
- Vapour pressure (Annex VII, 7.5.)
  i. Justification for use of a method outside its recommended range
  ii. Measured value of the vapour pressure for at least two temperatures
  iii. Log(P) versus 1/T curve
- Water solubility (Annex VII, 7.7.)
  i. Analytical method used for determination of the concentration(s)
- Partition coefficient n-octanol/water (Annex VII, 7.8.)
  i. reference substances used with their respective K_{OW} values
- Skin corrosion (Annex VII, 8.1.)
  i. Cell system used
  ii. Description of evaluation criteria used
  iii. Description of any modifications of the test procedure
  iv. Test doses used
  v. Description of other effects observed
- Skin sensitization (Annex VII, 8.3.)
  i. Dose levels: induction and challenge
  ii. Duration of exposure period
  iii. Interval between dosing
- Mutagenicity (Annex VII, 8.4.)
  i. Positive and negative control substances; basis for their selection

B) Pursuant to Articles 41(1)(a) and (b), 41(3), 12(1)(a), 10(a)(vi), and 13 (3) as well as Annex VII and Annex XI, Section 1.1.2, point (4) of the REACH Regulation the Registrant shall submit adequate and reliable documentation for the non standard study addressing the endpoint as follows:

- Eye irritation (Annex VII, 8.2.)
  i. Cell type or line used for the in vitro tests
  ii. Test system endpoints measure
  iii. Positive, vehicle, negative and benchmark control substances; basis for their selection
  iv. Acceptable response ranges for positive, vehicle and negative control substances, including their historical control data and basis for acceptable ranges
  v. Decision criteria for interpreting the outcome of a test result, basis for their decision criteria for classifying the chemical, accuracy characteristics of the selected decision criteria

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vi. Concentration selection procedure: defined limit concentration, range-finding studies, procedures for determining limit of solubility, highest non-cytotoxic concentration
vii. Duration of test article exposure, post-exposure incubation
viii. Exposure time-response curves
ix. The ET_{50} (the time of exposure to the test article that reduces MTT conversion by 50%)
x. Outcome of positive and negative controls

C) Pursuant to Articles 41(1)(a), 41(3), 10(a)(vi), 12(1)(a), and Annex VII of the REACH Regulation, the Registrant shall submit following information:

- Skin irritation (Annex VII, 8.1). The recommended test method is EU B.46 according to test guideline EpiSkin™, modified EpiDerm™, or SkinEthic HSE™.

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 **six months from date of decision**.

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, does not comply with the requirements of **Articles 10, 12, 13 and Annexes VII and XI** of the REACH Regulation. 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.

A) Pursuant to Articles 10(a)(vi), 12(1)(a) and (b) of the REACH Regulation, a registration for a substance produced in quantities of 1 – 10 tonnes per year shall contain as a minimum the information specified in Annex VII of the REACH Regulation. The technical dossier shall include study summaries for the information derived from application of Annex VII. A study summary is defined as "*summary of objectives, methods, results and conclusions of a full study report providing sufficient information to make an assessment of the relevancy of the study*" (Article 3(29)).

The submitted technical dossier does not provide sufficient information to make an assessment of the relevancy of the studies possible for the following endpoints missing the respective elements given below:

- Melting/freezing point (Annex VII, 7.2.)
  i. Type of method used
- Vapour pressure (Annex VII, 7.5.)
  i. Justification for use of a method outside its recommended range
  ii. Measured value of the vapour pressure for at least two temperatures
  iii. Log(P) versus 1/T curve
- Water solubility (Annex VII, 7.7.)
  i. Analytical method used for determination of the concentration(s)

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- Partition coefficient n-octanol/water (Annex VII, 7.8.)
  i. reference substances used with their respective K_{OW} values
- Skin corrosion (Annex VII, 8.1.)
  i. Cell system used
  ii. Description of evaluation criteria used
  iii. Description of any modifications of the test procedure
  iv. Test doses used
  v. Description of other effects observed
- Skin sensitization (Annex VII, 8.3.)
  i. Dose levels: induction and challenge
  ii. Duration of exposure period
  iii. Interval between dosing
- Mutagenicity (Annex VII, 8.4.)
  i. Positive and negative control substances; basis for their selection

B) Pursuant to Article 13(1) and (3), in conjunction with Annex XI, Section 1.1.2, point (4), existing data from non-standard test methods may be used, if "*adequate and reliable documentation is provided*".

Regarding eye-irritation the Registrant has provided results from a study using the EpiOcular™ Tissue Model. Since there is no recognised test method within the meaning of Article 13 (3) of the REACH Regulation available using the EpiOcular™ Tissue Model, the present test method must be considered as a non-standard method.

The submitted technical dossier does not provide adequate documentation to make an assessment of the adequacy and reliability of this non-standard test method as follows:

- Eye irritation (Annex VII, 8.2.)
  i. Cell type or line used for the in vitro tests
  ii. Test system endpoints measure
  iii. Positive, vehicle, negative and benchmark control substances; basis for their selection
  iv. Acceptable response ranges for positive, vehicle and negative control substances, including their historical control data and basis for acceptable ranges
  v. Decision criteria for interpreting the outcome of a test result, basis for their decision criteria for classifying the chemical, accuracy characteristics of the selected decision criteria
  vi. Concentration selection procedure: defined limit concentration, range-finding studies, procedures for determining limit of solubility, highest non-cytotoxic concentration
  vii. Duration of test article exposure, post-exposure incubation
  viii. Exposure time-response curves
  ix. The ET_{50} (the time of exposure to the test article that reduces MTT conversion by 50%)
  x. Outcome of positive and negative controls

C) According to Column 1 of Annex VII, Section 8.1, the assessment of skin irritation or corrosion shall comprise steps for assessing both skin corrosion and skin irritation in vitro.

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The technical dossier provided by the Registrant included a study assessing skin corrosion potential in vitro (EU test method B.40bis). The Registrant concluded that under these conditions the substance is non-corrosive.

ECHA concludes that the study provided by the Registrant does not cover the endpoint for skin irritation. This is because the test method (B.40bis) is not suitable for detecting skin irritation potential as it only addresses if the substance is corrosive or non-corrosive. The Registrant is accordingly requested to perform an in vitro study for assessing skin irritation to fulfil this information requirement. ECHA recommends use of the test method B.46 according to test guideline EpiSkin™, modified EpiDerm™ or SkinEthic HSE™.

The Registrant is requested to submit the missing elements for the endpoints as listed above (A to C) to make an assessment of the relevancy of the related studies possible.

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 adapted to the technical progress by Commission Regulation (EC) No 761/2009 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.

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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.

Done at Helsinki,

[redacted]

Jukka Malm
Director of Regulatory Affairs

European Chemicals Agency
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