ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-0000001752-76-06/F Helsinki, 28 February 2012

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 (REACH Regulation).

I. Procedure

Pursuant to Article 41(1) of the REACH Regulation the ECHA has performed a compliance check of the registration dossier for [redacted] submitted by [redacted] (Registrant), latest submission number [redacted], for 100 - 1000 tonnes per year.

The Registrant notified the substance pursuant to the national legislation implementing Directive 67/548/EEC relating to the classification, packaging and labelling of dangerous substances (as amended) by submitting a notification to the German competent authority in accordance with Article 7 of Directive 67/548/EEC. The notification number allocated was [redacted].

Article 24(1) of the REACH Regulation provides that the notification is regarded as a registration and ECHA has assigned a registration number.

The compliance check was initiated on 21 October 2010 following a tonnage band update to 100 – 1000 tonnes per year.

On 14 July 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 16 August 2011 the Registrant provided to ECHA comments on the draft decision.

ECHA reviewed the further information received and amended the statement of reasons of the draft decision. However, the final conclusions of the draft decision were not amended.

On 2 September 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, one Competent Authority of the Member States submitted a proposal for amendment to the draft decision. ECHA reviewed the proposal for amendment received and decided to modify the draft decision accordingly by requesting an additional study for the screening of reproductive/developmental toxicity.

On 5 October 2011 ECHA notified the Registrant of the proposal for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments within 30 days of the receipt of the notification.

On 17 October 2011, the draft decision was referred to the Member State Committee.

On 4 November 2011, the Registrant provided comments on the proposal for amendment. The Member State Committee took the comments of the Registrant into account.

After discussion in the Member State Committee meeting on 7-9 December 2011, the Member State Committee further modified the draft decision and a unanimous agreement of the Member State Committee on the further modified draft decision was reached on 8 December 2011.

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)(vii), 3(28), 13(3) and 111 as well as Sections 1.1.4. and 3.1.5. of Annex I to the REACH Regulation, the Registrant shall provide in the IUCLID format a robust study summary on the following endpoint:

1. Skin sensitisation - Local lymph node assay (Annex VII, Section 8.3. of the REACH Regulation): Information concerning the choice of dose levels used in the study, information about the results of the use of positive controls either in the study itself, or relevant historical data which validates the reliability of the study.

Pursuant to Articles 41(1)(a) and (b), 41(3), 10(a)(vi) and 12(1)(d), as well as Annexes VIII and XI of the REACH Regulation, the Registrant shall submit the information using the test method as indicated below.

2. Sub-chronic toxicity study (90-day) (Annex IX, 8.6.2. REACH Regulation), rodents, by the oral route (EU test method B.26) to be performed with the registered substance;

3. Screening for reproductive/developmental toxicity, one species (Annex VIII, 8.7.1 REACH Regulation) (OECD 421 test method) to be performed with the registered substance; and

4. Pre-natal developmental toxicity study (Annex IX, 8.7.2. REACH Regulation), one species, by the oral route (EU test method B.31) to be performed with the registered substance.

The Registrant shall determine the appropriate order of the studies taking into account the possible outcomes and considering the possibilities for adaptations of the standard information requirements according to column 1 or 2 provisions of the relevant Annexes of the REACH Regulation.

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 28 August 2014.

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

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 for the purpose of registration within the applicable tonnage band of 100 to 1000 tonnes per year in accordance with **Article 6** of the REACH Regulation, does not comply with the requirements of Articles **10, 12 and 13 and with Annexes VII and IX** 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.

Following the tonnage band update to 100-1000 tonnes per year for a substance previously notified under Directive 67/548/EEC, the Registrant is according to Article 24(2) of the REACH Regulation obliged to submit the additional required information corresponding to the reached tonnage threshold as well as to all lower tonnage thresholds in accordance with Articles 10 and 12 of the REACH Regulation.

1. Robust study summary for the local lymph node assay

According to Articles 10(a)(vii) and 111 and Sections 1.1.4 and 3.1.5 of Annex I to the REACH Regulation, a technical dossier that is in the IUCLID format shall include robust study summaries of all key data used in the human health and environmental hazard assessment. Under Article 3(28), the robust study summary shall include a "detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report."

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 ECHA (see section IV below for further details).

The Registrant has not reported in the IUCLID format robust study summary (RSS) within the meaning of Article 3(28) of the REACH Regulation for the local lymph node assay (LLNA) provided under the standard information requirement of Annex VII, Section 8.3 for skin sensitisation. In particular, the summary provided misses information concerning the choice of dose levels used in the study, information about the results of the use of positive controls either in the study itself, or relevant historical data which validates the reliability of the study, as explained below.

ECHA observes that the provided LLNA has been conducted by the Registrant according to EU test method B.42 to assess the skin sensitising potential of the registered substance. The study did not show a sensitising effect at dose levels up to and including 50% of the registered substance in acetone/olive oil. EU test method B.42 (SKIN SENSITISATION: LOCAL LYMPH NODE ASSAY), provides under section 1.3.2.3: "Existing acute toxicity and dermal irritation data should be considered, where available, in selecting the three consecutive concentrations so that the highest concentration maximises exposure whilst avoiding systemic toxicity and excessive local skin irritation" [Reference to: *Kimber, I., Derman, R.J., Scholes, E.W., and Basketter, D.A. (1994). The local lymph node assay: developments and applications. Toxicology, 93, p. 13-31*, and to EU test method B.4; ACUTE TOXICITY: DERMAL IRRITATION/CORROSION]. No information on dose selection in the LLNA study has been provided in the study summary or elsewhere in the registration dossier.

Furthermore, the Registrant has not submitted information on the reliability of the LLNA assay, as the IUCLID study summary provided does not include information on the use of a positive control group. According to EU test method B.42, each LLNA study should include positive controls to "demonstrate appropriate performance of the assay and competency of the laboratory to successfully conduct the assay". EU test method B.42 further states that while a positive control group is ordinarily required in each assay, "there may be situations in which test laboratories will have available historic positive control data to show consistency of a satisfactory response over a six-month or more extended period", and furthermore, that "In those situations, less frequent testing with positive controls may be appropriate at intervals no greater than six months".

The Registrant shall therefore submit a RSS in a IUCLID format of the LLNA study provided with information concerning the choice of dose levels used in the study, information about the results of the use of positive controls either in the study itself, or relevant historical data which validates the reliability of the study.

Further guidance can be found in the *Information requirements Manual 1 Requirements for Robust Study Summary* published on the website at:
http://echa.europa.eu/doc/publications/practical_guides/pg_report_robust_study_summaries.pdf

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

A sub-chronic toxicity study (90-day) is a standard information requirement of Annex IX, Section 8.6.2 at the present tonnage level.

ECHA notes that the Registrant has provided an oral 28-day study in rat (Annex VIII, 8.6.1), and in its comments to the draft decision a justification for omitting this information requirement based on Annex XI, 3, substance tailored exposure-driven testing. Nevertheless according to Annex XI, 3.2.(a) (ii), footnote 1 a DNEL-derived from an 28-day study shall not be considered appropriate to omit a 90-day study. Therefore the conditions set out in Annex XI 3.2. (a) are not met. ECHA also points out that the Registrant has not demonstrated strictly controlled conditions for all exposure scenarios. Therefore the conditions set out in Annex XI 3.2. (b) are not met.

The Registrant shall therefore provide information on 90-day repeated dose toxicity by the oral route in rodents with the registered substance using the EU test method B.26.

3. Screening for reproductive/developmental toxicity

A screening study for reproductive/ developmental toxicity (OECD 421) is an information requirement under the REACH Regulation (Annex VIII, 8.7.1).

ECHA notes that the Registrant has provided a waiver for reproductive toxicity with a justification in accordance with Annex XI, section 3, of the REACH Regulation, based on negligible exposure. Contrary to the adaptation from the standard information requirement presented by the Registrant, the information in the Chemical Safety Report on the registered substance does not reflect the provisions of Annex XI, section 3 of the REACH Regulation.

On the basis of Annex VIII 8.7.1 column 2 of the REACH Regulation, a screening study for reproductive /developmental toxicity may not need to be conducted if a pre-natal developmental toxicity study is available. This condition is not fulfilled as at this moment a study on prenatal developmental toxicity is not available. Therefore ECHA considers this dossier as not fulfilling the standard information requirements under Annex VIII, 8.7.1 of the REACH Regulation.

The Registrant shall perform a screening study for reproductive/ developmental toxicity for one species with the registered substance according to test method OECD 421. The results of the study should be taken into account when considering the need to continue further reproductive toxicity testing including the pre-natal developmental toxicity study (EU Test Method B.31).

4. Pre-natal developmental toxicity study

A study for pre-natal developmental toxicity in one species is a standard information requirement of Annex IX, Section 8.7.2 at the present tonnage level. A decision on the need to perform a study at this tonnage level or the next on a second species should be based on the outcome of the first test and all other relevant available data.

ECHA observes that the Registrant suggests to omit the pre-natal developmental toxicity study, and justifies this by referring to the provisions of Annex XI, section 3 of the REACH Regulation governing substance-tailored exposure-driven testing, whereby testing in accordance with sections 8.6 and 8.7 of Annex VIII and in accordance of with Annex IX and Annex X may be omitted based on the exposure scenario(s) developed in the chemical safety report (CSR) (section 3.1). In the justification the Registrant states that a closed system technology applies for the manufacturing and processing of the registered substance, and that exposure is therefore negligible. Secondary exposure is considered also to be negligible, according to the Registrant, as no wastewater results from manufacturing and processing of the registered substance. Also, the process water will be recycled in a closed system. During normal use, the registered substance is incorporated in polymer matrix, and exposure is deemed to be negligible, according to the Registrant.

ECHA notes that in its comments to the draft decision the Registrant illustrates his efforts to strive for a safe use of the chemical. Nevertheless, the rules for adaptation from the standard information requirement set out in Annex XI, 3 have not been fulfilled:

- A relevant DNEL (Annex XI, 3.2.(a)(ii)) could not be derived because no data on toxicity to development is included in the dossier; it is not possible to substitute these provisions by results of e.g. a 28-day study (or screening study for reproductive/developmental toxicity, c.f. footnote of Annex XI 3.2 a (ii)). Therefore the conditions in Annex XI 3.2 (a) are not met.
- The Registrant has not demonstrated strictly controlled conditions for all exposure scenarios. Therefore the conditions of Annex XI 3.2. (b) are not met.

As the justification presented by the Registrant does not comply with Annex XI, section 3.1, and no other valid argument to omit the information requirement has been presented, the Registrant shall provide information on pre-natal developmental toxicity by the oral route in one species with the registered substance using EU test method B.31. A decision on the need to perform a study at this tonnage level or the next on a second species should be based on the outcome of the first test and all other relevant available data.

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5. Deadline for submitting the required information

In the draft decisions communicated to the Registrant the time indicated to provide the requested information was 12 months from the date of adoption of the decision. As the decision now also requests for information on a screening study on reproductive/ developmental toxicity ECHA considers that a reasonable time period for providing the remaining required information in the form of an updated IUCLID5 dossier is 30 months from the date of the adoption of the decision. The decision was therefore modified accordingly.

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 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.

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