ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 03.10.2012

Decision number: TPE-D-0000002516-75-07/F

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

For N-methylaniline, CAS No 100-61-8 (EC No 202-870-9), 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 proposals submitted as part of the jointly submitted registration dossier in accordance with Articles 10(a)(ix) and 12 (1)(e) thereof for N-methylaniline, CAS No 100-61-8 (EC No 202-870-9), by [redacted] (Registrant), latest submission number [redacted], for the tonnage band of 1000 tonnes or more per year:

- Subchronic dermal toxicity: 90-d study (OECD 411);
- Two-generation reproduction toxicity study (OECD 416).

The present decision relates to the examination of the testing proposals for repeated dose 90-day dermal toxicity study. The testing proposal for the two-generation reproductive toxicity study is addressed in a separate decision although all testing proposals were initially addressed together in the same draft decision.

On 1 April 2011, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of nine testing proposals set out by the Registrant in the registration dossier for the substance mentioned above (at that time the latest submission number was [redacted]).

ECHA held a third party consultation for the testing proposals from 1 July until 15 August 2011. ECHA did receive information from third parties.

Subsequently to an informal communication between ECHA and the Registrant on 25 November 2011 regarding testing that was already ongoing, the Registrant submitted dossier updates on 17 November 2011, 11 January 2012 and 15 March 2012 removing seven of the nine previously submitted testing proposals.

Information received from third parties related to the remaining testing proposal on the sub-chronic toxicity study is considered in Section III below.

On 27 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 29 May 2012 ECHA received comments from the Registrant.

The comments are reflected in the Statement of Reasons (Section III) whereas no amendments to the Testing Required (Section II) were made.

On 14 June 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 submitted proposals for amendment to the draft decision. None of them concerned the request for the sub-chronic toxicity study.

On 18 July 2012 ECHA notified the Registrant of proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on those proposals for amendment within 30 days of the receipt of the notification.

ECHA reviewed the proposals for amendment received and decided not to amend the draft decision.

On 30 July 2012 ECHA referred the draft decision to the Member State Committee.

The Registrant did not provide any comments on the proposed amendments.

The draft decision was split into two draft decision documents: one relating to the testing proposal for a two-generation reproductive toxicity study and one relating to the testing proposal for a sub-chronic toxicity (90-day) study.

A unanimous agreement of the Member State Committee on the draft decision relating to the sub-chronic toxicity study was reached on 3 September 2012 in a written procedure launched on 22 August 2012 and ECHA took the decision pursuant to Article 51(6) 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.

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 method and the registered substance subject to the present decision:

> Sub-chronic toxicity study (90-day) in rats, oral route (Annex IX, 8.6.2.; test method: EU B.26/OECD 408)

while the originally proposed test for a sub-chronic toxity study (90-day), dermal route (test method: EU B.28/OECD 411) 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 **3 April 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 and scientific information submitted by third parties.

Sub-chronic toxicity study (90-day)

a) Examination of the testing proposal

Pursuant to Article 40(3)(d) of the REACH Regulation, ECHA may reject a proposed test and pursuant to Article 40(3)(c) of the REACH Regulation, ECHA may require the Registrant to carry out one or more 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 provide information for this endpoint.

The Registrant proposed testing via the dermal route (OECD 411). In light of the limited uptake via the dermal route and the absence of an appropriate dermal toxicity study which could serve as a dose-range finding study for the 90-day toxicity study, ECHA considers that testing by the dermal route is not the most appropriate. ECHA considers that testing via the oral route is the most appropriate since oral uptake is significantly higher than after dermal administration, the available oral 28-day toxicity study can be used as a dose-range finding study for the proposed 90-day study and there are no indications for a relevant first-pass effect after oral administration which could limit route-to-route extrapolation. Furthermore, the oral 90-day study can serve as a dose-range finding study for the proposed two-generation reproductive toxicity study. In addition, it will give a sound basis to derive the long-term inhalation DNEL which is based on analogy to human effects observed with aniline.

The Registrant provided comments on the draft decision expressing consent to conduct an oral sub-chronic toxicity study and outlining arguments for other routes of administration. The default route for testing is the oral route. ECHA evaluated the appropriateness of testing by the dermal and inhalation route according to the criteria set out in Annex IX, 8.6.2, column 2. Taking into account the likelihood of dermal and inhalation human exposure, ECHA concluded that these routes are not as appropriate for testing as the oral route.

The Registrant did not specify the species to be tested. According to the test method EU B.26/OECD 408 the rat is the preferred rodent species. ECHA considers this species as being appropriate.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation. For the reasons explained further below the information provided by third parties is not sufficient to fulfil this information requirement.

Third party information:

The third party has proposed a strategy for ECHA to consider before further tests on animals are requested. More specifically, it suggested that consideration should be given to existing data in context of a category approach (cp. Monocyclic Aromatic Amines Category in test plan for US EPA). However, third parties were invited, as specified by Article 40(2) of the REACH Regulation to submit "scientifically valid information and studies that address the relevant substance and hazard end-point, addressed by the testing proposal". As the proposal for a strategy as such cannot be regarded information or studies, ECHA concludes that this is not a sufficient basis to fulfil the data/information requirement.

Furthermore, in the proposed read-across approach as an element of the strategy the third party did not demonstrate that human health effects of the registered substance may be predicted from data on reference substances. Although ECHA recognises that the information as provided by the third party might be scientifically valid, it does not fulfil Annex XI, 1.5. requirements and is therefore not sufficient to allow ECHA to reject the testing proposal. Nevertheless, ECHA acknowledges that the Registrant may himself supplement under his own responsibility the argumentation and information provided by the third party in order to make use of any adaptation possibilities.

c) Outcome

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, oral route (test method: EU 26/OECD 408) using the registered substance, whereas the proposed test (sub-chronic toxity study (90-day), dermal route; test method: EU B.28/OECD 411) is rejected in accordance with Article 40(3)(d) 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.

d) Deadline for submitting the information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 30 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also requested a reproductive toxicity study according to the standard information requirement of Annex X, 8.7.3. of the REACH Regulation. As the testing proposal for this study is not addressed in the present decision, ECHA considers that a reasonable time period for providing the required information in the form of an updated IUCLID5 dossier is 18 months from the date of the adoption of the decision. The decision was therefore modified accordingly.

IV. Adequate identification of the composition of the tested material

The process of evaluation of testing proposals set out in Article 40 of the REACH Regulation

aims at ensuring that the new studies meet real information needs. Within this context, the Registrant's dossier was sufficient to confirm the identity of the substance to the extent necessary for evaluation of the testing proposal. The Registrant must note, however, that this information has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In addition, it is important to ensure that the particular sample of substance tested in the new studies 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 covers different grades, the sample used for the new studies must be suitable to assess these.

Finally, there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the studies 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).

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.

[redacted]

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