EUROPEAN CHEMICALS AGENCY

Helsinki, 5 July 2019

Addressee: [redacted]

Decision number: TPE-D-2114465667-34-01/F
Substance name: N-methylaniline
EC number: 202-870-9
CAS number: 100-61-8
Registration number: [redacted]
Submission number: [redacted]
Submission date: 15/02/2018
Registered tonnage band: 100-1000

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation ((EC) No 1907/2006) (the REACH Regulation), ECHA examined your testing proposal(s) and decided as follows.

Your following testing proposals are rejected:

1. **Sub-chronic toxicity study (90-day), dermal route (Annex IX, Section 8.6.2.; test method: OECD TG 411) in rats using the registered substance.**
2. **Extended one-generation toxicity study (Annex IX, Section 8.7.3.; test method: OECD 443) in rats, oral route using the registered substance.**

The reasons for this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by Wim De Coen, Head of Unit, Hazard Assessment.

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons

The decision of ECHA is based on the examination of the testing proposals submitted by you and scientific information submitted by third parties.

1. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(d) of the REACH Regulation, ECHA may reject a proposed test.

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.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the dermal route according to OECD TG 411.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Sub-chronic toxicity (90 day): dermal. ECHA has taken these considerations into account. In your considerations on adaptation possibilities, you briefly suggest that read-across to two other substances might be applicable "*Therefore, the argumentation here which aimed initially to justify the need for a test shows that an alternative solution can be found, based on read-across approach on aniline and N,N-dimethylaniline, if it is considered enough robust by ECHA*". However, no further read-across justifications were included in the registration dossier.

You proposed testing by the dermal route. The dermal route might be appropriate for testing following the criteria set out in Annex IX, Section 8.6.2, column 2. However, in light of the more limited uptake via the dermal route, ECHA considers the oral route, which is the preferred route, as most appropriate.

ECHA notes that the registered substance has a harmonized classification as STOT RE2 under Regulation (EC) No 1272/2008. A reliable short-term toxicity study (28 days) by the oral route is available showing severe toxicity effects according to the criteria for classifying the substance as R48, for which the observed NOAEL-28 days, with the application of an appropriate uncertainty factor, allows the extrapolation towards the NOAEL-90 days for the same route of exposure (oral) as well as for the dermal route. Therefore, as also pointed out in a third party comment below, ECHA considers that the criteria of Annex IX, Section 8.6.2, column 2, first indent, are met and a sub-chronic toxicity study (90 days) does not need to be conducted.

Therefore, ECHA rejects your testing proposal.

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 might be sufficient to fulfil this information requirement.

A third party has indicated that the registered substance has a harmonized classification for specific target organ toxicity following repeated exposure (STOT RE2) according to

Regulation (EC) No 1272/2008. The third party refers to the ECHA REACH Guidance R.7a, according to which a 90-day study is 'usually required', but does not need to be conducted if a 28-day study is available showing severe toxicity sufficient to classify the substance for STOT RE and where the NOAEL (with the application of an appropriate assessment factor) allows the extrapolation of a 90-day NOAEL.

As explained above, ECHA agrees that an adaptation according to Annex IX, Section 8.6.2., column 2, first indent, can be accepted.

c) Outcome

Therefore, your proposed test for Sub-chronic toxicity study (90-day), dermal route (Annex IX, Section 8.6.2.; test method: OECD TG 411) is rejected according to Article 40(3)(d) of the REACH Regulation.

You are requested to update your registration dossier in the relevant sections with an adaptation according to Annex IX, Section 8.6.2., column 2, first indent, to indicate that a reliable oral short-term toxicity study (28 days) with the registered substance shows severe toxicity effects sufficient to classify the substance for specific target organ toxicity, for which the observed NOAEL-28 days, with the application of an appropriate uncertainty factor, allows the extrapolation towards the NOAEL-90 days and to update your CSR, accordingly.

2. Extended one-generation reproductive toxicity study (Annex IX, Section 8.7.3.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(d) of the REACH Regulation, ECHA may reject a proposed test.

You have submitted a testing proposal for a two-generation reproductive toxicity study according to EU B.35./OECD TG 416 with the following justification: "*N-methylaniline (NMA) registration dossier was first submitted by the company* [redacted] *at > 1000 tpy. However, due to a lack of data, the registration dossier was rejected by ECHA. Indeed, two tests, submitted each to a testing proposal, were required by the Agency for the completeness of the dossier: a 90-day repeated dose toxicity by oral route (OECD 408) and a two-generation reproductive toxicity study (OECD 416) or extended one-generation reproductive study (OECD 443).*
The toxicity to reproduction test is only performed if the 90-day repeated dose toxicity study by oral route indicates adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity.
[redacted] *decided not to perform these tests because they were too expensive.* [redacted] *finally chose to cease the manufacturing of NMA. The registration was stopped and no longer required by ECHA.*
More recently, the company [redacted] *decided to register NMA at the tonnage 100-1000 tpy. The role of Lead Registrant was transferred from* [redacted] *to* [redacted]*, which bought the data of NMA registration dossier to* [redacted]*. ECHA lowered the Joint submission tonnage band to allow* [redacted] *submitting its dossier".*

According to Annex IX, Section 8.7.3., as amended by Commission Regulation (EU) 2015/282 (entered into force on 13 March 2015), a two-generation reproductive toxicity study is no information requirement any longer. However, the requirement according to Annex IX, Section 8.7.3., i.e. the extended one-generation reproductive toxicity study, is

only an information requirement if adverse effects on reproductive organs or tissues have been observed in the available repeated dose toxicity studies (e.g. a 28-day or 90-day repeated dose toxicity study, OECD TG 421 or 422 screening studies) or if they reveal other concerns in relation with reproductive toxicity.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (extended one-generation reproductive toxicity study). ECHA notes that you provided your considerations and you applied read-across to fulfil the respective information requirement. ECHA has taken these considerations into account. In your considerations on adaptation possibilities, you briefly suggest that read-across to two other substances might be applicable *"Therefore, the argumentation here which aimed initially to justify the need for a test shows that an extended one-generation reproductive toxicity study or two-generation reproductive toxicity study might not be necessary to conduct, if ECHA judges that it is enough robust. Indeed, no evidence of fertility adverse effects were observed from the repeated dose toxicity studies of two analogues of NMA, i.e. aniline and N,N-dimethylaniline"*. However, no robust read-across justifications were included.

ECHA notes that you have not included any justification why to perform a reproductive toxicity study at tonnage level 100 – 1000 tonnes per year. According to Annex IX, Section 8.7.3., an extended one-generation reproductive toxicity study is an information requirement if adverse effects on reproductive organs or tissues have been observed in the available repeated dose toxicity studies (e.g. a 28-day or 90-day repeated dose toxicity study, OECD 421 or 422 screening studies) or if they reveal other concerns in relation with reproductive toxicity. For the substance subject to the present decision there is a short-term repeated dose toxicity study (28 days) provided in the registration dossier that does not indicate adverse effects on reproductive organs or tissues or other concerns.

ECHA considers that the proposed study is at this stage not necessary to fulfil the information requirement of Annex IX, Section 8.7.3. of the REACH Regulation because no adverse effects on reproductive organs or tissues or other concerns in relation with reproductive toxicity have been observed in a short-term repeated dose toxicity study.

Therefore, ECHA rejects you testing proposal.

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 might be sufficient to fulfil this information requirement.

A third party has indicated that the tonnage level of the registered substance only requires the conduct of a reproduction toxicity study if the 28-day or 90-day study indicates adverse effects on reproductive organs or tissues.

As explained above, ECHA agrees that based on the information requirements of Annex IX, Section 8.7.3. of the REACH Regulation, it is not necessary to perform the proposed study.

c) Outcome

Therefore, your proposed two-generation reproductive toxicity study according to EU B.35./OECD TG 416 is rejected according to Article 40(3)(d) of the REACH Regulation.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposals for examination in accordance with Article 40(1) on 14 February 2018.

ECHA held a third party consultation for the testing proposals from 23 April 2018 until 7 June 2018. ECHA received information from third parties (see Appendix 1).

This decision does not take into account any updates after **14 November 2018**, 30 calendar days after the end of the commenting period.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision and invited you to provide comments.

ECHA did not receive any comments by the end of the commenting period.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided in your registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

2. Failure to comply with the requests in this decision will result in a notification to the enforcement authorities of the Member States.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition.

   In addition, it is important to ensure that the particular sample of the substance tested in the new tests 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 or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.