EUROPEAN CHEMICALS AGENCY

Helsinki, 14 December 2016

Addressee: [redacted]

Decision number: CCH-D-2114350027-58-01/F
Substance name: N-[3-(dimethylamino)propyl]methacrylamide
EC number: 226-002-3
CAS number: 5205-93-6
Registration number: [redacted]
Submission number: [redacted]
Submission date: 10.07.2013
Registered tonnage band: >1000T

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA requests you to submit information on

1. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2, column 2; test method: EU B.31/OECD TG 414) in a second species (rabbits), oral route with the registered substance;**

2. **Ready biodegradability (Annex VII, Section 9.2.1.1; test method: DOC die-away test, OECD TG 301A)**

   or

   Ready biodegradability (Annex VII, Section 9.2.1.1; test method: CO2 evolution test, OECD TG 301B);

   or

   Ready biodegradability (Annex VII, Section 9.2.1.1; test method: MITI test (I), OECD TG 301C);

   or

   Ready biodegradability (Annex VII, Section 9.2.1.1; test method: Closed bottle test, OECD TG 301D);

   or

   Ready biodegradability (Annex VII, Section 9.2.1.1; test method: Modified OECD screening test, OECD TG 301E);

   or

   Ready biodegradability (Annex VII, Section 9.2.1.1; test method: Manometric respirometry test, OECD TG 301F);

   or

Ready biodegradability (Annex VII, Section 9.2.1.1; test method: Ready biodegradability – CO2 in sealed vessels (headspace test), OECD TG 310);

with the registered substance;

3. **Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2; test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25/OECD TG 309) at a temperature of 12 °C with the registered substance;**

4. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: generate an exposure assessment for all scenarios (1-9) and revise the risk characterisation accordingly.**

5. **Identification of DNEL(s) and risk characterisation (Annex I, Section 1.4. and 6.): revise long-term DNEL(s) for workers inhalation and dermal route systemic effects using the assessment factors recommended by ECHA and revise the risk characterisation accordingly *or* provide a detailed justification for not using the recommendations of ECHA Guidance R.8 for DNEL derivation;**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

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 another study (extended one-generation reproductive toxicity study, Annex X, Section 8.7.3). As 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 registration dossier is **22 October 2018** (22 months from the date of the adoption of the decision). The decision was therefore modified accordingly.**You shall also update the chemical safety report, where relevant.**

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

Appeal

For the final decision: 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, shall 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[2] by Kevin Pollard, Head of Unit, Evaluation E1

[2] 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

In your comments to the draft decision you have stated that "an update of some parts of the registration dossier would be needed". You indicate the substance is used as intermediate and would be consumed in industrial uses (co-monomer in the production of coating polymers, the service life ending with the polymerisation process).In this regard, ECHA notes that the registration dossier subject to dossier evaluation is not limited to intermediate uses. The uses include professional end use in formulations and consumer end use in formulations.

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2., column 2) in the second species

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

Pre-natal developmental toxicity studies on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

The technical dossier contains information on a pre-natal developmental toxicity study in rats by the oral route using the registered substance as test material. However, there is no information provided for a pre-natal developmental toxicity study in a second species.

With regard to your comment to update the registration with a test proposal ECHA considers that you agree to undertake the testing. However, as a compliance check decision making procedure is ongoing, no new testing proposal needs to be submitted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

The test in the first species was carried out by using a rodent species (rats). According to the test method EU B.31/OECD 414, the rabbit is the preferred non-rodent species. On the basis of this default assumption, ECHA considers that the test should be performed with rabbits as a second species.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a second species (rabbits) by the oral route.

Notes for your consideration

The dose selection for the study provided in the first species ([redacted], 2013) does not strictly follow the criteria set in OECD TG 414 or in EU B.31, which states that highest dose should be chosen with the aim to induce some developmental and/or maternal toxicity (clinical signs or a decrease in body weight), but no death and suffering. The dose levels selected are well below the limit dose set in the test guideline (1000 mg/kg bw/day) and no maternal and/or developmental effects were observed in the study.

The highest dose level should be aimed to produce slight toxicity to allow comparison of effect levels and effects of developmental toxicity with those of systemic toxicity.

3. Ready biodegradability (Annex VII, Section 9.2.1.1.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

"Ready biodegradability" is a standard information requirement as laid down in Annex IX, section 9.2.1.1. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have provided a study record for a biodegradation test performed according to OECD TG 301 C. However, the information provided in the registration dossier is not appropriate to conclude that the registered substance is readily biodegradable.

You indicate in your rationale for the reliability in the robust study summary: "*Guideline study, but not reported in detail*".

Article 14(1) in conjunction with Annex I and Article 10(a)(vii) of the REACH Regulation require to provide the information derived from the application of Annexes VII to XI in the form of a robust study summary (RSS). In accordance with Article 3(28) of the REACH Regulation, a robust study summary means "*a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment on the study minimising the need to consult the full study report*".

Indeed, details on the study results are missing from your robust study summary. More specifically the following information is not reported or not reported in sufficient detail:

- test material;
- study design: sludge adaptation, details on inoculum (including sampling site, concentration, pre-conditioning, adaptation), parameter followed for biodegradation estimation, details on analytical methods, details on study design, reference substance, darkness, pH, CEC, oxygen conditions, sampling and analytical measurements details); the initial concentration is also slightly unclear ("*To avoid toxic effects the test substance was diluted 1:2500*");
- results: lag phase, replicate values, graphs and/or result tables, information on the 10-day window, assessment of potential inhibition, reference substance test results; in the results section, only the degradation % after day 4, 5, 6, 8, 23 is given.

Therefore, the information provided in the robust study summary is insufficient and does not allow an independent assessment of the adequacy of this study, its results and use for hazard assessment (see also ECHA Practical Guide 3: How to report robust study summaries, version 2.0 – November 2012: http://echa.europa.eu/documents/10162/13643/pg_report_robust_study_summaries_en.pdf).

ECHA therefore considers that the information provided on this endpoint is in its current form not adequate to conclude on ready biodegradability.
In your comments you note that you agree to perform a biodegradation test. You also mention that you "*are confident that this test will confirm the results of the available study, which has a somewhat limited documentation.*"

Regarding the test method, depending on the substance profile, you may conclude on ready biodegradability, by applying the most appropriate and suitable test guideline among those listed in the ECHA Guidance on information requirements and chemical safety assessment, Volume 5 Chapter R7b (May 2008) and in the paragraph below. The test guidelines include the description of their applicability domain.

Therefore, in case you would not be in a position to update the RSS with the missing information outlined above and explained in ECHA Practical Guide 3: How to report robust study summaries, version 2.0 – November 2012: http://echa.europa.eu/documents/10162/13643/pg_report_robust_study_summaries_en.pdf, with the information you currently have, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to perform one of the following tests with the registered substance subject to the present decision:

Ready biodegradability (Annex VII, 9.2.1.1.; test method: DOC die-away test, OECD 301A)
or
Ready biodegradability (Annex VII, 9.2.1.1.; test method: CO2 evolution test, OECD 301B)
or
Ready biodegradability (Annex VII, 9.2.1.1.; test method: MITI test (I), OECD 301C)
or
Ready biodegradability (Annex VII, 9.2.1.1.; test method: Closed bottle test, OECD 301D)
or
Ready biodegradability (Annex VII, 9.2.1.1.; test method: Modified OECD screening test, OECD 301E)
or
Ready biodegradability (Annex VII, 9.2.1.1.; test method: Manometric respirometry test, OECD 301F)
or
Ready biodegradability (Annex VII, 9.2.1.1.; test method: Ready biodegradability – CO2 in sealed vessels (headspace test), OECD 310).

4. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

"Simulation testing on ultimate degradation in water" is a standard information requirement as laid down in Annex IX, section 9.2.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

Column 2 of Section 9.2.1.2 of Annex IX further indicates that the study does not need to be conducted if the substance is highly insoluble in water or if the substance is readily biodegradable.

You have sought to adapt this information requirement according to Annex IX, Section 9.2.1.2., column 2. You provided the following justification for the adaptation: "*According to Annex IX 9.2.1.2. Column 2, a study on biodegradation in water and sediment does not need to be conducted as N-[3(dimethylamino)propyl] methacrylamide is readily biodegradable (experimental result please see chapter 5.2.1. biodegradation screening test according to OECD 301 C).*"

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.2.1.2., column 2. As explained under section 3 above, there is no reliable data currently available in the dossier to conclude on the ready biodegradability of the substance. Therefore, the adaptation cannot be accepted.

ECHA further notes that the substance is not highly insoluble in water either.

As the substance is not likely to adsorb (low logKow, logKoc) and is water soluble, ECHA considers the OECD TG 309 to be appropriate to fulfil the endpoint.

ECHA notes that due to lack of information on the degradation of the substance you have not in your CSA or the technical dossier justified that there is no need to investigate further the degradation of the substance or its degradation products.

Therefore, your adaptation of the information requirement cannot be accepted.

However, as explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

In your comments on the draft decision you have noted: "*We are confident that a simulation test will not be necessary because not only the available biodegradation study showed rapid biodegradation but also the two starting material in the synthesis of DMAPMA, methacrylamide and dimethylaminopropylamine, are both regarded as readily biodegradable.*" ECHA concludes that you intend to adapt the specific requirement based on the results of screening biodegradation testing and available information. Following the re-evaluation of the biodegradation screening test, as required by this decision, you may need to revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation. If you conclude that no further biodegradation testing is required, you can update your technical dossier specifically for those information requirements that depend on biodegradability with a scientifically justified adaptation, which ECHA will evaluate in the follow up phase. ECHA does acknowledge that a substance being readily biodegradable is a valid adaptation to this information requirement according to Column 2 of Annex IX section 9.2.1.2

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 2.0, November 2014) Aerobic mineralisation in surface water – simulation biodegradation (test method EU C.25. / OECD TG 309) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.2.

One of the purposes of the simulation test is to provide the information that must be considered for assessing the P/vP properties of the registered substance in accordance with Annex XIII of REACH regulation to decide whether it is persistent in the environment. Annex XIII also indicates that "*the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions*". The Guidance on information requirements and chemical safety assessment R.7b (version 2.0, November 2014) specifies that simulation tests "attempt to simulate degradation in a specific environment by use of indigenous biomass, media, relevant solids [...], and a typical temperature that represents the particular environment". The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-9 (version 2.1 October 2012) indicates 12°C (285K) as the average environmental temperature for the EU to be used in the chemical safety assessment. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD 307, OECD 308 and OECD 309. Therefore, the test should be performed at the temperature of 12°C and, in line with REACH Annex IX, Section 9.2.3., identification of degradation products should also take place.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Aerobic mineralisation in surface water – simulation biodegradation test (test method: EU C.25./OECD TG 309) at a temperature of 12°C.

5. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation, the registration shall contain a chemical safety report (CSR) which shall document the chemical safety assessment conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

ECHA notes that you have classified the substance as skin irritation 2, eye damage 1, skin sensitiser 1 and thus, fulfilling the criteria set out in Article 14(4) of the REACH Regulation to require an exposure assessment and a risk characterisation in the chemical safety assessment. In accordance with Article 14(4), the CSR must include an exposure assessment and risk characterisation, due to the substance being classified.

Annex I section 5 of the REACH Regulation requires to generate exposure scenarios and exposure estimations for the substances meeting the criteria as set out in Article 14(4) of the REACH Regulation. The exposure assessment shall consider all stages of the life-cycle of the substance resulting from the manufacture and identified uses and shall cover any exposures that may relate to the identified hazards. The additional steps of the CSA shall be carried out in accordance with Sections 5 (for Exposure assessment) and 6 (for Risk characterisation) of Annex I of the REACH Regulation."

Annex I section 6 of the REACH Regulation requires to characterise the risk for each exposure scenario and consider the human population (exposed as workers, consumer or indirectly via the environment and if relevant a combination thereof) and the environmental spheres for which exposure to the substance is known or reasonable foreseeable, under the assumption that the risk management measures described under exposure scenario have been implemented. In addition, the overall environmental risk caused by the substance shall be reviewed by integrating the results for the overall releases, emissions and losses from all sources to all environmental compartments.

ECHA's Guidance on information requirements and chemical safety assessment, Part B: Hazard Assessment, Section B.8.4. (pages 47 to 48) (version 2.1, December 2011) states that "*if no adverse effects have been observed in studies at the highest recommended concentration/doses tested, this would normally indicate that no hazard has been identified and no DNEL or PNEC can be derived and hence exposure assessment for that route of exposure, type of effect or protection target would not be needed*".

In the CSR you provided, the exposure assessment for the environment is missing. You claimed that no exposure assessment is necessary for the environment by stating that "*As no environmental hazard was identified no environmental-related exposure assessment and risk characterization was performed.*"

ECHA notes that you have classified the substance and that effects were observed in some environmental toxicity studies. In particular, in the long-term toxicity study to aquatic invertebrates a 21 day NOEC reproduction of 25 mg/L was obtained, in the study on aquatic plants a 72h EC50 (growth rate) of 94.2 mg/L was obtained, in the short-term study on fish an 96h LC50 of 290 mg/L was obtained and in the short-term toxicity study to aquatic invertebrates a 48h EC50 of 272 mg/L was obtained. Therefore, adverse effects have been observed below the highest recommended concentrations tested.

In your comments you agree to update the registration with an environmental risk assessment. ECHA acknowledges your agreement to provide the requested information which will be taken into account by ECHA in the follow up phase.

With regard to the scope of the required exposure assessment, as stated above and in accordance with Annex I, section 5.0., it has to cover all hazards that have been identified according to sections 1 to 4 of Annex I of REACH Regulation.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to generate an environmental exposure assessment for all scenarios (1-9) and revise the risk characterisation accordingly.

6. Identification of DNEL(s) and risk characterisation (Annex I, Sections 1.4. and 6.)

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation, the registration shall contain a chemical safety report (CSR) which shall document the chemical safety assessment (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

Annex I, Section 1.4.1 of the REACH Regulation requires that the following factors shall, among others, be taken into account when deriving DNELs:

a. the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;
b. the nature and severity of the effect;
c. the sensitivity of the human (sub-)population to which the quantitative and/or qualitative information on exposure applies;
d. and that the DNELs reflect the likely route(s), duration and frequency of exposure.

The ECHA Guidance on information requirements and chemical safety assessment Chapter R.8 provides further details and specifically provides default factors which should be applied to derive DNELs in the absence of substance specific information to fulfil the REACH obligations.

ECHA notes that the assessment factors (AF) applied were not derived in accordance to the default assessment factors recommended in the ECHA Guidance R.8 for DNEL derivation.

Specifically, in both calculations for the two long-term systemic DNELs (dermal and inhalation) you have applied AFs which are not in line with the default factors listed in the ECHA Guidance. The intraspecies differences for workers has been reduced from 5 to 3, and the AF accounting for the remaining interspecies differences (factor 2.5) has not been used.

ECHA notes that the reference to the ECETOC guidance cannot replace the ECHA Guidance which has been agreed between all stakeholders, including industry representatives.

As explained above, the information provided on DNEL for the registered substance in the chemical safety report does not meet the general provisions for preparing a chemical safety report as described in Annex I, 1.4.1.

Consequently, you are given two options: you shall revise the DNELs for workers by applying the assessment factors recommended by ECHA that are appropriate in this case as specified above. Subsequently, you shall re-assess related risks.

In the alternative, you shall, in accordance with Annex I, Section 1.4.1, provide a full justification for the DNELs derived for workers provided in the chemical safety report by specifying how the following has been taken into account:

a. the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;
b. the nature and severity of the effect;
c. the sensitivity of the human (sub-)population to which the quantitative and/or qualitative information on exposure applies;
d. and that the DNELs reflect the likely route(s), duration and frequency of exposure.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to revise long-term DNEL(s) for workers inhalation and dermal route systemic effects using the default assessment factors and other recommendations of ECHA Guidance R.8 for DNEL derivation and revise the risk characterisation accordingly *or* provide a detailed justification for not using the recommendations of ECHA Guidance R.8 for DNEL derivation.

Notes for your consideration

The results of the studies requested with this decision shall be taken into account when revising the DNELs.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 09 October 2015.

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

ECHA took into account your comments and changed Appendix I: Reasons.

ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment.
ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s).

ECHA referred the draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

The present decision relates solely to a compliance check requesting information in form of a pre-natal developmental toxicity study (Annex X, 8.7.2.), studies on ready biodegradability (Annex VII, Section 9.2.1.1), simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2), exposure assessment and risk characterisation (Annex I, Sections 5. and 6.), identification of DNEL(s) and risk characterisation (Annex I, Section 1.4. and 6.). The other compliance check requirement of an extended one-generation reproductive toxicity study (Annex X, Section 8.7.3), is addressed in a separate decision although all endpoints were initially addressed together in the same draft decision.

After discussion in the Member State Committee meeting on 25-28 October 2016, unanimous agreement of the Member State Committee on the draft decision related to endpoints other than extended-one generation reproductive toxicity (Annex X, 8.7.3.), as modified at the meeting, was reached on 27 October 2016. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This compliance check decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

2. Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In carrying out the test(s) required by the present decision it is important to ensure that the particular sample of substance tested 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 test(s) must be suitable to assess these. Furthermore, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.