Decision number: TPE-D-2114322159-53-01/F Helsinki, 30 March 2016

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

For N-(2-hydroxypropyl)oleamide, EC No 203-828-2 (CAS No 111-05-7), 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 registration dossier in accordance with Articles 10(a)(ix) and 12(1)(d) thereof for N-(2-hydroxypropyl)oleamide, EC No 203-828-2 (CAS No 111-05-7), submitted by [redacted] (Registrant).

- 90-day repeated dose oral toxicity study (OECD 408);
- Developmental toxicity / teratogenicity study (OECD 414);
- Fish early-life stage (FELS) toxicity test (OECD 210);
- Toxicity to soil macroorganisms (OECD 222).

This decision is based on the registration as submitted with submission number [redacted], for the tonnage band of 100 to 1000 tonnes per year.

This decision does not take into account any updates after 2 October 2015, i.e. 30 calendar days after the end of the commenting period.

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 registration at a later stage.

ECHA received the registration dossier containing testing proposals for further examination pursuant to Article 40(1) on 22 May 2013. The registration was subsequently updated on 25 March 2015 containing the above-mentioned testing proposals.

ECHA held a third party consultation for the testing proposals from 14 August 2014 until 28 September 2014. ECHA did not receive information from third parties.

On 27 July 2015 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

By 02 September 2015 the Registrant did not provide any comments on the draft decision to ECHA.

On 21 January 2016 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 for amendment of the draft decision within 30 days of the receipt of the notification.

As no proposal for amendment was submitted, ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

II. Testing required

A. Tests required pursuant to Article 40(3)

The Registrant shall carry out the following proposed tests pursuant to Article 40(3)(a) and 13(4) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26/OECD 408) in rats;
2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31/OECD 414) in rats or rabbits, oral route;
3. Fish, early-life stage (FELS) toxicity test (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage toxicity test, OECD 210);
4. Long-term toxicity on terrestrial invertebrates (Annex IX, Section 9.4.1., column 2; test method: Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*), OECD 222).

The Registrant shall carry out the following additional tests pursuant to Article 40(3)(c) and 13(4) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

5. Long-term toxicity testing on plants (Annex IX, Section 9.4.3., column 2); test method: Terrestrial plants, growth test (OECD 208), with at least six species tested (with as a minimum two monocotyledonous species and four dicotyledonous species) or test method: Soil Quality – Biological Methods – Chronic toxicity in higher plants (ISO 22030);

6. Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: Soil microorganisms: nitrogen transformation test, EU C.21/OECD 216).

Pursuant to Articles 41(1), 41(3), 10(b) and 14 as well as Annex I of the REACH Regulation, once the results of the above terrestrial studies are available to the Registrant, he shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation, including an updated derivation of the terrestrial PNEC (Predicted No-Effect Concentration).

Note for consideration by the Registrant:

The Registrant 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 to and conforming with the appropriate rules in the respective Annex, and an adequate and reliable documentation.

Failure to comply with the requests in this decision, or to fulfil otherwise the information requirements with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

B. Deadline for submitting the required information

Pursuant to Articles 40(4) and 22(2) of the REACH Regulation, the Registrant shall submit to ECHA by **6 April 2018** an update of the registration dossier containing the information required by this decision, including, where relevant, an update of the Chemical Safety Report. The timeline has been set to allow for sequential testing as appropriate.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposals submitted by the Registrant for the registered substance.

A. Tests required pursuant to Article 40(3)

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

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the 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 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 has submitted a testing proposal for a sub-chronic toxicity study (90 day) by the oral (EU B.26/OECD 408) route to be performed with the registered substance subject to the present decision.

ECHA considers that the proposed study by the oral route is appropriate to fulfil the information requirement of Annex IX, Section 8.6.2. of the REACH Regulation because the proposed route is the most appropriate route of administration having regard to the likely route of human exposure due to the following reasons.

The Registrant proposed testing by the oral route. In light of the physic-chemical properties of the substance (paste liquid with low vapour pressure not classified as corrosive/irritating to the skin or damaging/irritating to the eyes) and the information provided on the uses and human exposure (no uses with spray application), ECHA considers that testing by the oral route is most appropriate.

The Registrant did not specify the species to be used for testing. According to the test method EU B.26/OECD 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

b) Outcome

Therefore, pursuant to Article 40(3)(a)of the REACH Regulation, the Registrant is requested to carry out the proposed study with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD 408).

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

A pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. 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 has submitted a testing proposal for a pre-natal developmental toxicity study according to EU B.31/OECD 414 to be performed with the registered substance subject to the present decision.

ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

The Registrant did not specify the species to be used for testing. He did not specify the route for testing. According to the test method EU B.31/OECD 414, the rat is the preferred rodent species, the rabbit the preferred non-rodent species and the test substance is usually administered orally. ECHA considers these default parameters appropriate and testing should be performed by the oral route with the rat or the rabbit as a first species to be used.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is requested to carry out the proposed study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in rats or rabbits, oral route (test method: EU B.31/OECD 414)

3. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. 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 has submitted a testing proposal for testing the registered substance for long-term toxicity testing on fish, Fish, early-life stage toxicity test, OECD 210, with the following justification: "*The registered substance is slightly soluble in water (WS < 1 mg/l), so chronic aquatic tests have been proposed (OECD 210) or performed (OECD 211 and OECD 201).*" ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 9.1.6 of the REACH regulation.

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), Chapter R7b (Section R.7.8.5 including Figure R.7.8-4), if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. There is no information on the short-term toxicity of the substance to aquatic invertebrates and fish available in the registration dossier. Thus, there were no indications in the dossier that the fish would be substantially more or less sensitive than aquatic invertebrates or algae.

b) Outcome

Therefore, pursuant to Article 40(3)(a)of the REACH Regulation, the Registrant is required to carry out the proposed study using the registered substance subject to the present decision: Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.; test method: Fish, early-life stage toxicity test, OECD 210).

c) Notes for consideration by the Registrant

Due to the low solubility of the substance in water and high adsorptio potential of the substance OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA Guidance, Chapter R7b, table R. 7.8-3 summarising aquatic toxicity testing of difficult substances should be consulted by the Registrant for choosing the design of the requested long-term ecotoxicity tests and for calculation and expression of the result of this test.

4. – 6. Effects on terrestrial organisms (Annex IX, Section 9.4.)

Pursuant to Article 40(3)(a) and (c) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test and to carry out additional tests in cases of non-compliance of the testing proposal with Annexes IX, X or XI.

The Registrant must address the standard information requirements set out in Annex IX, section 9.4., for different taxonomic groups: effects on soil micro-organisms (Annex IX, section 9.4.2.), short-term toxicity testing on invertebrates (Annex IX, section 9.4.1.), and short-term toxicity testing on plants (Annex IX, section 9.4.3.). Column 2 of section 9.4 of Annex IX specifies that long-term toxicity testing shall be considered by the Registrant instead of short-term, in particular for substances that have a high potential to adsorb to soil or that are very persistent.

The information on the endpoint 'effects on terrestrial organisms' is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements.

1) Terrestrial Invertebrates (Annex IX, Section 9.4.1. and Column 2 of Annex IX, Section 9.4.)

a) Examination of the testing proposal

The Registrant proposed a long-term toxicity test on terrestrial invertebrates (Earthworm Reproduction Test (Eisenia fetida/Eisenia andrei), OECD 222), with the following justification: "*The terrestrial species tested should cover three taxonomic groups (plants, invertebrates and micro-organisms) as defined in Annex IX, but also different pathways of exposure (e.g. feeding, surface contact). Earthworm testing allows potential uptake via each of surface contact, soil particle ingestion and porewater. A long test earthworm test is proposed as the Log Koc value is high.*" As the substance has a high potential to adsorb ECHA agrees that long-term testing is indicated (Column 2 of Section 9.4. of Annex IX). The proposed test is suitable to address the information requirement of Annex IX, section 9.4.1.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study using the registered substance subject to the present decision: Long-term toxicity testing on invertebrates (Annex IX, Section 9.4.1. and Column 2 of Annex IX, Section 9.4.; test method: Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*), OECD 222).

2) Terrestrial Plants (Annex IX, Section 9.4.3. and Column 2 of Annex IX, Section 9.4.)

The proposed test accepted by ECHA under subsection (1) above is not sufficient by itself to address the standard information requirements of Annex IX, section 9.4.3. ECHA notes that the registration dossier does not contain data for this endpoint.

The Registrant proposed to adapt this standard information requirement with the following justification: "*The terrestrial species tested should cover three taxonomic groups (plants, invertebrates and micro-organisms) as defined in Annex IX, but also different pathways of exposure (e.g. feeding, surface contact). Earthworm testing allows potential uptake via each of surface contact, soil particle ingestion and porewater. So terrestrial plant testing is not necessary.*" However, as noted by ECHA above long-term toxicity test with soil invertebrates is not sufficient by itself to address the standard information requirements of Annex IX, section 9.4.3.

According to section R.7.11.5.3., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), substances that are ionisable or have a log K_{ow}/K_{oc} >5 are considered highly adsorptive, whereas substances with a half-life >180 days are considered very persistent in soil. Furthermore, the substances that have effect concentrations EC/LC50 <1 mg/L for algae, *Daphnia* or fish are considered very toxic to aquatic organisms.

Based upon the available aquatic toxicity information (72h ErC50 for algae is 0.11 mg/L) and the physico-chemical properties (log Kow is 6.39) of the substance, and in relation to section R.7.11.6., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), ECHA considers that the substance would fall into soil hazard category 4. For such substances it is not possible to adapt the present standard information requirement depending on the results of the other long-term study for soil requested by the present decision and an initial screening assessment based upon the Equilibrium Partitioning Method (EPM). The Guidance foresees that long-term toxicity tests according to the information requirements of Annex X should be carried out and that the lowest value obtained should be used to derive the PNEC soil.

High adsorption potential of the substance indicates the need for long-term testing to be performed (Column 2 of Section 9.4. of Annex IX). No argument has been provided as to why long-term testing is not appropriate. Furthermore, ECHA Guidance on information requirements and chemical safety assessment Chapter R10, section R.10.6.2. (version May 2008) allows the potential application of a lower assessment factor (AF) if information on additional long-term terrestrial toxicity test of two trophic levels were available. In contrast, the Guidance does not allow for a lower AF to be applied if information on a short-term study were to become available in addition to the long-term invertebrate study, which ECHA accepted under subsection (1) above. Therefore ECHA concludes that considering the properties of the substance only a long-term toxicity test on plants (and not the short-term) will provide the necessary information.

OECD guideline 208 (Terrestrial plants, growth test) considers the need to select the number of test species according to relevant regulatory requirements, and the need for a reasonably broad selection of species to account for interspecies sensitivity distribution. For long-term toxicity testing, ECHA considers six species as the minimum to achieve a reasonably broad selection. Testing shall be conducted with species from different families, as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD 208 guideline. The Registrant should consider if testing on additional species is required to cover the information requirement.

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is required to carry out one of the following additional studies using the registered substance subject to the present decision: Long-term toxicity testing on plants (Annex IX, Section 9.4.3. and Column 2 of Annex IX, Section 9.4.; test method: Terrestrial plants, growth test, OECD 208, with at least six species tested (with as a minimum two monocotyledonous species and four dicotyledonous species) or Soil Quality – Biological Methods – Chronic toxicity in higher plants, ISO 22030).

3) Soil microorganisms (Annex IX, section 9.4.2.)

The hazard to soil microbial communities is a standard information requirement under Annex IX, section 9.4.2. of the REACH Regulation. ECHA notes that the registration dossier does not contain data for this endpoint and that the proposed test that ECHA accepted under subsection (1) above is not sufficient to address this standard information requirement.

The Registrant proposed to adapt this standard information requirement with the following justification: "*The terrestrial species tested should cover three taxonomic groups (plants, invertebrates and micro-organisms) as defined in Annex IX, but also different pathways of exposure (e.g. feeding, surface contact). Earthworm testing allows potential uptake via each of surface contact, soil particle ingestion and porewater. Furthermore, the substance is readily biodegradable. So soil microorganisms testing is not necessary.*" However, as noted by ECHA above long-term toxicity test with soil invertebrates is not sufficient by itself to address the standard information requirements of Annex IX, section 9.4.2.

ECHA concludes that the effects on soil microorganisms need to be ascertained by performing a relevant test (test method: EU C.21/OECD 216).

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is required to carry out the following additional study using the registered substance subject to the present decision: Effects on soil microorganisms (Annex IX, section 9.4.2.; test method: Soil microorganisms: nitrogen transformation test, EU C.21/OECD 216).

IV. Adequate identification of the composition of the tested material

The process of examination 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 examination 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 grade(s) registered to enable the relevance of the studies to be assessed.

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 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://www.echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

Authorised[2] by Claudio Carlon , Head of Unit, Evaluation

[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.