EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114295022-56-01/F Helsinki, 23 March 2015

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

For 4-(1-methyl-1-phenylethyl)-N-[4-(1-methyl-1-phenylethyl)phenyl]aniline, CAS No 10081-67-1 (EC No 233-215-5), 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 4-(1-methyl-1-phenylethyl)-N-[4-(1-methyl-1-phenylethyl)phenyl]aniline, CAS No 10081-67-1 (EC No 233-215-5), submitted by [redacted] (Registrant).

- Repeated Dose 90-Day Oral Toxicity in Rodents (OECD Guideline 408);
- *Daphnia magna* Reproduction Test (OECD Guideline 211);
- Earthworm, Acute Toxicity Tests (OECD Guideline 207).

This decision is based on the registration dossier 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 30 October 2014, the date upon which ECHA notified its draft decision to the Competent Authorities of the Member States pursuant to Article 51(1) 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 registration at a later stage.

ECHA received the registration dossier containing the above-mentioned testing proposals for further examination pursuant to Article 40(1) on 8 April 2013.

ECHA held a third party consultation for the testing proposal from 18 February 2014 until 4 April 2014. ECHA did not receive information from third parties.

On 19 August 2014 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 25 September 2014 the Registrant did not provide any comments on the draft decision to ECHA.

On 30 October 2014 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.

Subsequently, proposals for amendment to the draft decision were submitted.

On 5 December 2014 ECHA notified the Registrant of the proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on the proposals for amendment within 30 days of the receipt of the notification.

The ECHA Secretariat reviewed the proposals for amendment received and amended the draft decision.

On 15 December 2014 ECHA referred the draft decision to the Member State Committee.

By 5 January 2015 the Registrant did not provide any comments on the proposals for amendment.

A unanimous agreement of the Member State Committee on the draft decision was reached on 19 January 2015 in a written procedure launched on 9 January 2015.

ECHA took the decision pursuant to Article 51(6) 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. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211);

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:

3. Effects on terrestrial organisms:
    a) Long-term toxicity to terrestrial invertebrates (Annex IX, 9.4., column 2); test method: Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*), OECD 222, or Enchytraeid reproduction test, OECD 220, or Collembolan reproduction test in soil, OECD 232.
    b) Effects on soil micro-organisms (Annex IX, 9.4.2.; test method: Soil microorganisms: nitrogen transformation test, EU C.21/OECD 216);
    c) Long-term toxicity testing on plants (Annex IX, 9.4., 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 Soil Quality – Biological Methods – Chronic toxicity in higher plants, ISO 22030.

Note for the consideration of 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 **30 September 2016** an update of the registration dossier containing the information required by this decision, including, where relevant, an update of the Chemical Safety Report.

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) via the oral route (OECD 408) with the following justification: "*The lead registration dossier is for a substance manufactured or imported at > 100 t/a. Effects are noted in the 28-day study, that whilst not resulting in classification, do warrant further investigation. Therefore a a testing proposal for a 90-day repeated dose toxicity study in accordance with Section 8.6.2 of column 1, Annex IX is included.*"

ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 8.6.2. of the REACH Regulation. The Registrant proposed testing by the oral route. ECHA notes that the registered substance has a low vapour pressure and a particle size distribution not indicating a high potential for inhalation exposure. In light of the physico-chemical properties of the substance and the information provided on the uses and human exposure, 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. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

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 aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. 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 long-term toxicity study on aquatic invertebrates (*Daphnia magna* reproduction test, OECD 211) with the following justification: "*The substance demonstrates no effects on aquatic organisms at the limit of solubity in water in acute studies. However the CLP Regulation (EC No 1272/2008) states that Aquatic Chronic 4 is applicable to substances in:*
Cases when data do not allow classification under the above criteria but there are nevertheless some grounds for concern. This includes, for example, poorly soluble substances for which no acute toxicity is recorded at levels up to the water solubility (note 3), and which are not rapidly degradable and have an experimentally determined BCF≥500 (or, if absent, a log Kow≥4), indicating a potential to bioaccumulate, will be classified in this category unless other scientific evidence exists showing classification to be unnecessary. Such evidence includes chronic toxicity NOECs > water solubility or > 1 mg/l, or evidence of rapid degradation in the environment.
The substance fulfills this criteria in that no scientific data apart from QSAR exists to dispute the bioaccumulation potential assigned to the substance. As such, the registrant proposes to conduct an assessment of daphnia reproduction, in order to derive an appropriate NOEC for use in the removal of the Chronic Category 4 classification."

ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 9.1.5. of the REACH Regulation. However, ECHA notes that the 'grounds for concern' as explained under the criterion for classification as Aquatic Category Chronic 4 are not removed by performing only a long-term study with *Daphnia*. As it is not proven that the *Daphnia* is more sensitive than fish and there are no results from fish long-term toxicity testing, the classification would still remain valid.

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 1.2., November 2012), 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 were no indications in the dossier from the short-term toxicity studies on aquatic species that the fish would be substantially more sensitive than aquatic invertebrates. In such case, according to the integrated testing strategy, the *Daphnia* study is to be conducted first. If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, long-term fish testing may need to be conducted.

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 aquatic invertebrates (Annex IX, 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211).

c) Notes for consideration by the Registrant

Once results of the proposed test on long-term toxicity to aquatic invertebrates are available, the Registrant shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation. If the revised chemical safety assessment indicates the need to investigate further the effects on aquatic organisms, the Registrant shall submit a testing proposal for a long-term toxicity test on fish in order to fulfil the standard information requirement of Annex IX, 9.1.6. If the Registrant comes to the conclusion that no further investigation of effects on aquatic organisms is required, he shall update his technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex IX, 9.1.6.

Due to the low solubility of the substance in water and high potential for adsorption 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 test and for calculation and expression of the result of this test.

3. Effects on terrestrial organisms (Annex IX, Section 9.4.)

Pursuant to Article 40(3)(d) and (c) of the REACH Regulation, ECHA may reject a proposed test and require the Registrant to carry out other 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: short-term toxicity testing on invertebrates (Annex IX, section 9.4.1.), effects on soil micro-organisms (Annex IX, section 9.4.2.), 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.

a) Terrestrial Invertebrates (Annex IX, 9.4.1.)

The Registrant proposed a short-term toxicity test on terrestrial invertebrates (OECD 207), with the following justification: *"As significant adsorption to soil/sediment is predicted for the substance, an assessment of toxicity to soil macro-organisms is deemed appropriate in order to assess this endpoint in more detail. As such, an acute toxicity to Earthworm study is proposed to assess this endpoint. This is based on the fact that whilst the substance can be considered to have a high potential to absorb to soil, it is not proposed to be harmful to environmental organisms. As such, acute toxicity rather than long-term toxicity is appropriate for assessment."* This test is in principle suitable to address the standard information requirement of Annex IX, section 9.4.1.

However, according to section R.7.11.5.3., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (May 2008), 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 (or, if no information on half-life in soil is available, not readily biodegradable) are considered very persistent in soil. ECHA notes that, according to the evidence presented within the Registration dossier, the substance has a high potential to adsorb to soil ($logK_{oc}$ is 6.54) and is likely to be very persistent (the default setting for not readily biodegradable, when no DT_{50} in soil available) and therefore meets the column 2 adaptation criteria of Annex IX, section 9.4. concerning the use of long-term testing instead of short-term. Thus, ECHA concludes that considering the properties of the substance only a long-term toxicity test on invertebrates (and not the short-term) will provide the necessary useful information.

The earthworm reproduction test (OECD 222), Enchytraeid reproduction test (OECD 220), and Collembolan reproduction test (OECD 232) are each considered capable of generating information appropriate for the fulfilment of the information requirements for long-term toxicity testing to terrestrial invertebrates. ECHA is not in a position to determine the most appropriate test protocol, since this decision is dependent upon species sensitivity and substance properties.

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is required to carry out one of the following additional studies: Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*), OECD 222, or Enchytraeid reproduction test, OECD 220, or Collembolan reproduction test in soil, OECD 232, using the registered substance, while the short-term toxicity test on terrestrial invertebrates (OECD 207) is rejected pursuant to Article 40(3)(d) of the REACH Regulation,

b) Effects on soil microorganisms (Annex IX, 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 a) above is not sufficient to address this standard information requirement.

The Registrant proposed to adapt this standard information requirement with following justification: *"An assessment of earthworm toxicity is proposed for the substance; hence it is deemed not appropriate at the current time to assess for toxicity to soil micro-organisms. The substance is not intended to be released directly to the environment; and as such, diverse release from use of the various product categories will be the only source of exposure. In addition, the substance is not proposed to be hazardous to environmental organisms and demonstrates no toxicity to STP micro-organisms. As such, an assessment of soil macro-organisms is considered appropriate to assess the potential to cause a hazard to the terrestrial environment endpoint at the time."*

Based on information provided in the registration dossier ECHA considers that the exposure of soil by the registered substance is not unlikely (e.g. via consumer use of lubricants in open systems). Furthermore, the claim that the substance is not hazardous to environmental organisms is not substantiated by the data in the registration dossier. Thus, as noted above the test accepted by ECHA under subsection (a) is not sufficient by itself to address the standard information requirements of Annex IX, section 9.4.2. and the proposed adaptation of the standard information requirement is not acceptable.

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

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

ECHA emphasises that the intrinsic properties of soil microbial communities are not addressed through the EPM extrapolation method and therefore the potential adaptation possibility outlined for the information requirement of Annex IX, Section 9.4.3. does not apply for the present endpoint.

c) Terrestrial Plants (Annex IX, 9.4.3.)

The proposed test accepted by ECHA under subsection a) 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 following justification: *"An assessment of earthworm toxicity is proposed for the substance; hence it is deemed not appropriate at the current time to assess for toxicity to terrestrial plants. The substance is not intended to be released directly to the environment; and as such, diverse release from use of the various product categories will be the only source of exposure. In addition, the substance is not proposed to be hazardous to environmental organisms. As such, an assessment of soil macro-organisms is considered appropriate to assess the potential to cause a hazard to the terrestrial environment endpoint at the time."*

Based on information provided in the registration dossier ECHA considers that the exposure of soil by the registered substance is not unlikely (e.g. via consumer use of lubricants in open systems). Furthermore, the claim that the substance is not hazardous to environmental organisms is not substintiated by the data in the registration dossier. Thus, as noted above the test accepted by ECHA under subsection a) is not sufficient by itself to address the standard information requirements of Annex IX, section 9.4.3. and the proposed adaptation of the standard information requirement is not acceptable.

According to section R.7.11.6., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (May 2008), where there is adequate data available to sufficiently derive a PNEC for aquatic organisms, this PNEC can be used in a screening assessment for soil risks through the use of the Equilibrium Partitioning Method (EPM) approach.

ECHA notes that the Registrant has proposed a toxicity test on aquatic invertebrates (section III.A.2. of the present Decision) and that the results of this proposed test may lead to a revision of the currently derived PNEC aquatic. Therefore, ECHA considers that accurate allocation of an appropriate soil hazard category according to table R7.11-2, of the above mentioned guidance, is not possible at this time. Consequently, it is not possible to waive the standard information requirements for the terrestrial compartment through an initial screening assessment based upon the EPM, mentioned in Column 2 of Annex IX, section 9.4. Since a screening assessment for terrestrial organisms is not possible, testing for effects on all terrestrial organisms indicated in section 9.4. of Annex IX is considered necessary.

ECHA considers based on the substance properties as discussed under subsection (a) above, that the substance has a high potential to adsorb to soil ($logK_{oc}$ is 6.54) and is likely to be very persistent (the default setting for not readily biodegradable, when no DT_{50} in soil available). High potential to adsorb and persistence of the substance indicates the need for long-term testing to be performed (Column 2 of Section 9.4. of Annex IX). At this tonnage level, according to column 2 the registrant shall consider long-term testing. No argument has been provided in the dossier as to why, despite the potential to adsorb and persistence of the substance, long-term testing is not appropriate. 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 useful information. 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.

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 and testing shall be conducted, as a minimum with two monocotyledonous species and four dicotyledonous species. 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: 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), using the registered substance

If the results of the proposed toxicity test on aquatic invertebrates allow the subsequent derivation of a PNECwater, the Registrant may consider the ITS as recommended in section R.7.11.6., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (May 2008), and determine the need for further testing on terrestrial organisms.

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, or the information submitted by other registrants of the same substance, has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In relation to the proposed tests, the sample of substance used for the new studies must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is within the specifications of the substance composition that are given by the joint registrants. It is the responsibility of all joint registrants of the same substance to agree to the tests proposed (as applicable to their tonnage level) and to document the necessary information on their substance composition.

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 by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new studies must be suitable to assess these grades.

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.

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Claudio Carlon
Head of Unit, Evaluation