Decision number: TPE-D-2114300032-77-01/F Helsinki, 13 May 2015

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

For octamethyltrisiloxane, CAS No 107-51-7 (EC No 203-497-4), 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 octamethyltrisiloxane, CAS No 107-51-7 (EC No 203-497-4), submitted by [redacted] (Registrant).

- Prenatal Developmental Toxicity Study (OECD 414), rat, oral route via gavage, with the registered substance
- Soil Microorganisms: Nitrogen Transformation Test (OECD 216), with the registered substance
- Earthworm Reproduction Study (Eisenia fetida/Eisenia Andrei) (OECD 222), with the registered substance
- Terrestrial Plants Test: Seedling Emergence and Seedling Growth Test (OECD 208), with the registered substance

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 5 March 2015, 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 updated registration dossiers containing the above-mentioned testing proposals for further examination pursuant to Article 40(1) on 16 April 2013 and 6 February 2014.

ECHA held a third party consultation for the testing proposal from 3 March 2014 until 17 April 2014. ECHA did not receive information from third parties.

On 27 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. That draft decision was based on submission number [redacted].

On 29 August 2014 the Registrant updated his registration dossier submission number [redacted]. On 3 October 2014 ECHA received comments from the Registrant on the draft decision.

The ECHA Secretariat considered the Registrant's comments and the dossier update. The information is reflected in the Statement of Reasons (Section III) whereas no amendments to the Information Required (Section II) were made.

On 5 March 2015 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 Article 13(4) of the REACH Regulation using the indicated test method[s] and the registered substance subject to the present decision:

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31/OECD 414) in rats or rabbits, oral route.
2. Long-term toxicity testing on plants (Annex IX, 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)
3. Long-term toxicity to terrestrial invertebrates (Annex IX, 9.4.1., column 2); test method: Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*) OECD 222;
4. 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.

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 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 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 **20 May 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) on human health

1. 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 in rats according to EU B.31/OECD 414.

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 proposed testing in rats by the oral route. 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.

In the comments according to Art 50(1), the Registrant challenges the oral route he initially suggested and proposes the inhalation (vapour) route. However, ECHA notes that the testing proposal in the registration dossier remains for the oral route.

ECHA has assessed the available data afresh having regard to the likely route of human exposure, noting the Registrant's preference for the inhalation route, and taking into account the Registrant's comments.

ECHA considers that the test should be done by the oral route which is the most appropriate route for the following reasons:

1) REACH requires testing for reproductive toxicity at Annex IX and X, Section 8.7. by the "most appropriate route of administration, having regard to the likely route of human exposure".
2) ECHA Guidance on information requirements and chemical safety assessment,

Chapter R.7a: Endpoint specific guidance, indicates in Section R.7.6.1 that "it is important that the potential hazardous properties with respect to reproduction are established for chemicals with relevant human exposure that may be present in the environment, at the workplace and in consumer products." To establish reproductive hazard properties of the substance, systemic availability of the substance should be maximized. Systemic exposure is usually ensured by using the oral route as a route of exposure in testing.Therefore, ECHA considers the oral route as default route for reproductive toxicity studies to identify the reproductive hazard of a substance.

3) The Registrant indicated in his comments that the hazard assessment for repeated dose toxicity studies should not be different for that for the pre-natal developmental toxicity study. However, ECHA notes that hazard assessment for repeated dose toxicity and reproductive toxicity have different focusses. Hazard assessment for repeated dose toxicity studies following the REACH Regulation is dependent on the route of human exposure. Consequently, DNELs have to be derived for all relevant routes of human exposure. For derivation of such DNELs route-specific information is preferred or even required in case route-to-route extrapolation is not possible. However, hazard assessment for reproductive toxicity is intended to identify the reproductive hazard of a substance and DNELs for reproductive toxicity (pre-natal developmental toxicity and fertility) are not derived for a specific route of human exposure but usually by the oral route as indicated by the respective test methods (EU B.31/OECD 414). Therefore, the criteria for the selection of the most appropriate route of administration for testing are different. This difference is reflected in the REACH Regulation: for repeated dose toxicity studies conditions are provided in column 2 of Annex VIII, Section 8.6.1 and Annex IX, Section 8.6.2 when testing by inhalation or dermal route are appropriate. However, such criteria are not listed for reproductive toxicity studies according to Section 8.7. of Annexes VIII, IX or X.

Additionally, ECHA considers that there is evidence of sex-specific toxicity in the repeated-dose toxicity studies. Since the prenatal developmental toxicity study is performed in the female, ECHA has therefore evaluated the toxicity seen in female animals. The repeated-dose toxicity data shows that there are more severe systemic effects seen after oral administration in the 28-day study, compared to the effects seen after inhalation exposure in either an OECD 422 or 413 study. Specifically, in females, the liver weight increases were greater after oral, as compared to inhalation exposure, and increased hepatic porphyria/ periportal inflammation were only seen after oral administration, and not after inhalation exposure. The more severe systemic toxicity seen after oral exposure is a reason that the oral route is more appropriate than the inhalation route.

ECHA considers that the Registrant's arguments for choosing the inhalation route are not sufficient to establish that the inhalation route is most appropriate:

1) Even if the Registrant has mentioned some use patterns leading to inhalation exposure, human exposure to vapours is probably low, since the vapour pressure of the substance is reported at 25° C wiith 530 Pa.
2) In addition, the inhalation studies mentioned by the Registrant have been performed with heated vapours; e.g. in case of the 90-day sub-chronic toxicity study with vapours heated at 60-80 °C.

ECHA secretariat also notes that the conduct of oral studies is in general technically easier and incurs less expense than inhalation studies. In view of these reasons, ECHA secretariat considers that the oral route is the most appropriate route of administration for this study.

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).

B. Tests required pursuant to Article 40(3) on effects on terrestrial organisms

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.

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

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.

The Registrant proposed a long-term toxicity test on terrestrial plants ([OECD 208). According to section R.7.11.5.3., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (version 1.1, November 2012), 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. According to the evidence presented within the Registration dossier, the substance has a high potential to adsorb to soil ($\log K_{ow}$=6.6) and it is likely to be very persistent (0 % degradation in a 28 day ready biodegradation test according to OECD guideline 310) and therefore 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 9.4.3.

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.

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: Terrestrial plants, growth test (OECD 208), with at least six species tested (with as a minimum two monocotyledonous species and four dicotyledonous species).

3. Terrestrial Invertebrates (Annex IX, 9.4.1.)

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.

The Registrant proposed an Earthworm Reproduction Study (OECD 222).

The proposed test that ECHA has accepted under section 2 above can only address the information requirement of Annex IX, section 9.4.3. It is not sufficient by itself to address the standard information requirement of Annex IX, section 9.4.1. ECHA notes that the registration dossier does not contain data for this endpoint.

The registrant has considered that it is unfeasible, on the basis of the currently available information, to derive a PNEC for aquatic organisms. Consequently, it is not possible to waive the standard information requirements for the terrestrial compartment through an initial screening assessment based upon the Equilibrium Partitioning Method (EPM), mentioned in Column 2 of Annex IX, section 9.4. Consequently there is an information gap and it is necessary to provide information for the standard information requirement of Annex IX, Section 9.4.1.

By proposing a long-term toxicity test (accepted by ECHA under subsection 2 (b) above), ECHA considers that the Registrant has concluded on the need for long-term toxicity testing to be performed instead of short-term, on the basis that the substance meets the column 2 adaptation criteria of Annex IX, section 9.4. On this basis, ECHA considers that long-term testing is indicated (Column 2 of Section 9.4. of Annex IX). Moreover, section R.10.6.2., Chapter R10 of the abovementioned Guidance allows the potential application of a lower 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 plant study, which ECHA accepted under subsection 2 (b) above.

The earthworm reproduction test (OECD 222) is considered capable of generating information appropriate for the fulfilment of the information requirements for long-term toxicity testing to terrestrial invertebrates.

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: Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*) OECD 222.

4. Effects on soil microorganisms (Annex IX, 9.4.2.)

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.

The Registrant proposed a Soil Microorganisms: Nitrogen Transformation Test (OECD Guideline 216).

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 subsections 2 and 3 above are not sufficient to address this standard information requirement. ECHA concludes that the effects on soil microorganisms need to be ascertained. ECHA considers that a nitrogen transformation test (OECD 216) is suitable to address the information requirement of Annex IX, section 9.4.2.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the following additional study using the registered substance subject to the present decision: Soil microorganisms: nitrogen transformation test, EU C.21/OECD 216).

Note for the consideration of the Registrant

ECHA notes that in the endpoint study records of the testing proposals submitted the Registrant has explained that: *"the stability of test substance concentrations in the soil under realistic test conditions must be explored as part of method development."* ECHA agrees with the Registrant that in this case it is necessary to study the stability of test concentrations in soil and it may be necessary to modify the standard guidelines to allow the test substance concentrations to be maintained. Furthermore, ECHA notes that it is the Registrant's responsibility to design the tests in such a way that the effects to terrestrial organisms are adequately assessed.

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.

[redacted]

Claudio Carlon
Head of Unit, Evaluation