EUROPEAN CHEMICALS AGENCY

Helsinki, 19 July 2018

Addressee: [redacted]

Decision number: TPE-D-2114425319-49-01/F
Substance name: hexadecyltrimethoxysilane
EC number: 240-464-3
CAS number: 16415-12-6
Registration number: [redacted]
Submission number: [redacted]
Submission date: 05.07.2016
Registered tonnage band: 100-1000T

DECISION ON A TESTING PROPOSAL

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

Your testing proposal is accepted and you are requested to carry out:

1. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats using the registered substance.**

   It is at the Registrant's discretion to perform the intended additional examinations (i.e. *"examination of reproductive organs, sperm parameters, and oestrus cycle")* during the testing program.

2. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route using the registered substance.**

3. **Long-term toxicity to terrestrial invertebrates (Annex IX, Section 9.4.1., column 2; test method: Earthworm reproduction test (OECD TG 222)using the registered substance**

You are additionally requested to perform:

4. **Long-term toxicity testing on plants (Annex X, Section 9.4.6.; test method: Terrestrial plants, growth test, OECD TG 208 with at least six species tested (with as a minimum two monocotyledonous species and four dicotyledonous species) using the registered substance.**

5. **Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: Soil microorganisms: nitrogen transformation test, EU C.21./OECD TG 216) using the registered substance.**

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.

You are required to submit the requested information in an updated registration dossier by **27 July 2020**. You shall also update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

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

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[1] by Ofelia Bercaru, Head of Unit, Evaluation E3

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

Appendix 1: Reasons

The decision of ECHA is based on the examination of the testing proposal(s) submitted by you for the registered substance hexadecyltrimethoxysilane (EC No 240-464-3, CAS No CAS number: 16415-12-6) taking into account the updated dossier (submission number [redacted]).

ECHA notes that in the dossier with submission number [redacted] based on which the initial draft decision was prepared, you proposed an Earthworm acute toxicity test (EU C.8/OECD TG 207) to be performed on the registered substance. ECHA rejected this testing proposal and requested an Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*) (OECD 222) instead. In addition ECHA requested you to carry out a Terrestrial plants, growth test (OECD 208 or ISO 22030) and a Soil microorganisms test (EU C.21/OECD TG 216). In your updated dossier you have provided some changes to the testing strategy with respect to the environmental endpoints. ECHA has assessed your changed strategy in respect to these endpoints in sections 3. to 5. below.

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

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.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the oral route according to EU B.26/OECD TG 408 with the registered substance.

ECHA notes that in the updated dossier you provided your considerations for alternative methods to fulfil the information requirement for Sub-chronic toxicity (90-day): oral. You concluded that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

You proposed testing by the oral route. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA agrees that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, even though the information indicates that human exposure to the registered substance by the inhalation route is likely, there is no concern for severe local effects following inhalation exposure. Furthermore, ECHA points out that no repeated dose toxicity study by the oral route is available. Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

You proposed testing in rats. According to the test method EU B.26/OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

You proposed to extend the sub-chronic toxicity study (90 day) by examining additional parameters, including but not limited *to "examination of reproductive organs, sperm*

parameters, and oestrus cycle". ECHA notes, that it is at your discretion to perform the intended additional examinations during the testing program and use the results to ensure the safe use of the substance. However, you are reminded that the proposed extension of this study does not fulfil the standard information requirement in the registration dossier for reproductive toxicity set out in Annex X, Section 8.7.3.

In your comments to the draft decision you agreed to perform the requested study.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are 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 TG 408).

Notes for your consideration

ECHA notes that a revised version of OECD TG 408 was adopted this year by the OECD. This revised version contains enhancements of certain endocrine disrupting relevant parameters. You should test in accordance with the revised version of the guideline as published on the OECD website for adopted test guidelines (https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788).

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

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.

You have submitted a testing proposal for a pre-natal developmental toxicity study in rats according to EU B.31/OECD TG 414 by the oral route with the registered substance.

ECHA notes that in the updated dossier you provided your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (pre-natal developmental toxicity). You concluded that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

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

You proposed testing with the rat as a first species. According to the test method EU B.31/OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with the rat or rabbit as a first species.

You proposed testing by the oral route. ECHA agrees that the oral route is the most

appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

In your comments to the draft decision you agreed to perform the requested study.

Outcome

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

Notes for your consideration

For the selection of the appropriate species you are advised to consult ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017), Chapter R.7a, section R.7.6.2.3.2.

ECHA notes that a revised version of OECD TG 414 was adopted this year by the OECD. This revised version contains enhancements of certain endocrine disrupting relevant parameters. You should test in accordance with the revised version of the guideline as published on the OECD website for adopted test guidelines (https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788).

3. Long-term toxicity to terrestrial invertebrates (Annex IX, Section 9.4.1., column 2)

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

"Effects on terrestrial organisms" is a standard information requirement as laid down in Annex IX, Section 9.4. of the REACH Regulation. 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.). Furthermore, Annex IX, Section 9.4., column 2 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.

According to section R.7.11.5.3., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, June 2017), 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 (logK_{ow} 8.1). Therefore ECHA considers that a need for long-term testing is indicated (Column 2 of Section 9.4. of Annex IX).

The information on "long-term toxicity to invertebrates" 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.

In the updated dossier, you have submitted a testing proposal for a long-term toxicity test on terrestrial invertebrates (OECD 222) with the following justification: *"There are no data available on the chronic toxicity to terrestrial organisms of the registered substance. In order to fulfil the standard information requirements, a GLP-compliant study following OECD guideline 222 is proposed according to Annex IX and ECHA guidance R7c."*

ECHA notes that in IUCLID section 6.3.1. you have submitted as a key study an endpoint study record for an OECD Guideline 207 Earthworm, Acute Toxicity Test. However, due to the substance properties, as described above, the need for long term testing is indicated and ECHA agrees that such testing should be performed as proposed.
The earthworm reproduction test (OECD TG 222) proposed is considered capable of generating information appropriate for the fulfilment of the information requirements for long-term toxicity testing to terrestrial invertebrates.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are 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. Long-term toxicity to terrestrial plants (Annex IX, Section 9.4.3., column 2)

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

As already stated above, "effects on terrestrial organisms" is a standard information requirement as laid down in Annex IX, Section 9.4. of the REACH Regulation. 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.). Furthermore, Annex IX, Section 9.4., column 2 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 "short-term or long-term toxicity to plants" 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.

Neither the proposed test accepted by ECHA under point (3) nor the OECD 207 acute eartworm study already available in the updated registration dossier are sufficient by themselves 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.

In the dossier based on which ECHA prepared the initial draft decision (DD) you indicated that you would consider the need for toxicity testing of terrestrial plants based on the results obtained from the short-term earthworm study you proposed. ECHA rejected your adaptation and based on article 40(3)(c) requested long-term toxicity testing on plants (OECD 208 or ISO ISO 22030). ECHA notes that in your udpated dossier you have

submitted results obtained from an OECD 207 acute earthworm study, and a testing proposal for an OECD 222 chronic earthworm study.

In your updated dossier, you have proposed to adapt this standard information requirement by the following: *"In accordance with Regulation (EC) No 1907/2006, Column 2 of Annex IX and X, section 9.4, toxicity tests on terrestrial organisms do not need to be investigated if the outcome of the chemical safety assessment shows no indication of risk on terrestrial organisms from exposure to the substance in question. The PNEC soil has been derived using the equilibrium partitioning method on one hand and the result of a short term toxicity test on earthworm (OECD 207) on the other hand. In both cases, the risk characterization ratio (RCR) has demonstrated that there is no indication of risk i.e. PEC/PNEC soil < 1 from current exposure conditions to the test substance. In conclusion, in accordance to column 2 of Annex IX and X, section 9. 4 of Regulation (EC) No. 1907/2006, as the RCR soil is < 1 no further effects of the test substance on terrestrial organisms need to be investigated and consequently testing is thus omitted".*

ECHA notes that in your adaptation you indicate that there is no risk observed to the terrestrial compartment based on firstly PNECsoil derived using the equilibrium partitioning method (EPM) and secondly the results obtained from the acute earthworm study.

However, ECHA considers this approach not justified in this case for the reasons given below.

Firstly, it is not possible to use the EPM to assess the risks to terrestrial organisms in the circumstances of your case:

(i) due to absence of effects observed in the short-term aquatic studies available on the registered substance you have considered it unfeasible to derive a real PNECaquatic. Instead you have used the water solubility value of the proposed hydrolysis product of the registered substance as the basis for the derivation of PNECaquatic. ECHA considers that such PNEC cannot be used as basis of the EPM, another extrapolation method, to assess risks to the terrestrial organisms, (although it may be sufficient in some cases to derive a screen PNECaquatic).
(ii) The QSAR prediction submitted for the endpoint of hydrolysis cannot be considered reliable due to the registered substance being outside the parametric domain of the model as the molecular weight of the side chain is too large. It is hence not acceptable to use data on the proposed hydrolysis product as basis of assessing any potential risks to the environment.
(iii) Due to the low water solubility of the registered substance (water solubility of 0.002 mg/L) long-term aquatic toxicity testing is required to assess the risks of the registered substance to the aquatic environment (in accordance with column 2 of Annex VII and VIII, Section 9.1.). As you have only short-term aquatic data available such assessment cannot be made. In absence of adequate data on the aquatic environment it is not possible to use the aquatic data to adapt the information requirements for terrestrial toxicity testing.

Secondly, in addition to the EPM method you have used the PNECsoil derived from the acute earthworm study to conclude on no risks. This approach is not acceptable as ECHA *Guidance on information requirements and chemical safety assessment* (Chapter R 7C, version 3.0, June 2017) specifies that if only one study in combination with the EPM is used to conclude on terrestrial toxicity the single study needs to be a long-term study.

For the reasons described above it is not possible for you to waive the standard information requirements for the terrestrial compartment through the combined approach proposed by

you in your adaptation. Consequently there is an information gap and it is necessary to provide information for the standard information requirement of Annex IX, Section 9.4.3., column 2.

Based on the substance properties as discussed under point (3) above, ECHA considers that the substance has a high potential to adsorb to soil ($logK_{ow}$ 8.1). High absorbance 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 in the dossier as to why, despite the potential to adsorb, long-term testing is not appropriate. Therefore ECHA concludes that 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 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 TG 208 guideline. You 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, you are required to carry out one of the following additional studies 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), or Soil Quality – Biological Methods – Chronic toxicity in higher plants (ISO 22030).

5. Effects on soil micro-organisms (Annex IX, Section 9.4.2.)

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

As already stated above, "effects on terrestrial organisms" is a standard information requirement as laid down in Annex IX, Section 9.4. of the REACH Regulation. The Registrant must address the standard information requirements set out in Annex IX, Section 9.4., for different taxonomic groups taking into account substance properties: long-term toxicity testing on invertebrates (Annex IX, Section 9.4.1., column 2), effects on soil micro-organisms (Annex IX, Section 9.4.2.), and long-term toxicity testing on plants (Annex IX, Section 9.4.3., column 2).

You have sought to adapt the information requirement for "effects on soil micro-organisms". In the updated dossier you provided the following justification for the adaptation: " *In accordance with Regulation (EC) No 1907/2006, Column 2 of Annex IX and X, section 9.4, toxicity tests on terrestrial organisms do not need to be investigated if the outcome of the chemical safety assessment shows no indication of risk on terrestrial organisms from exposure to the substance in question. The PNEC soil has been derived using the equilibrium partitioning method on one hand and the result of a short term toxicity test on earthworm*

(OECD 207) on the other hand. In both cases, the risk characterization ratio (RCR) has demonstrated that there is no indication of risk i.e. PEC/PNEC soil < 1 from current exposure conditions to the test substance. In conclusion, in accordance to column 2 of Annex IX and X, section 9. 4 of Regulation (EC) No. 1907/2006, as the RCR soil is < 1 no further effects of the test substance on terrestrial organisms need to be investigated and consequently testing is thus omitted."." ECHA notes that the test that ECHA requested under point (3) above is not sufficient to address the standard information requirement of terrestrial toxicity and an adaptation of the information requirement for "effects on soil micro-organisms" is not valid. ECHA concludes that the effects on soil microorganisms need to be ascertained by performing a relevant test.

Furthermore, 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. would not apply for the present endpoint even if PNECaquatic were available. Nevertheless, ECHA notes that as fully discussed above in section (4) the approach proposed for assessing the risk to the terrestrial environment is not justified and cannot be accepted.

Therefore, your adaptation of the information requirement cannot be accepted. Consequently there is an information gap and it is necessary to provide information for this endpoint.

To address this endpoint, either a nitrogen transformation test (test method: EU C.21/OECD TG 216) or a carbon transformation test (test method: EU C.22/OECD TG 217) could be performed. According to Section R.7.11.3.1, Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, June 2017), ECHA considers the nitrogen transformation test (EU C.21/OECD TG 216) suitable for non-agrochemicals. For agrochemicals the carbon transformation test (EU: C.22/OECD TG 217) is also required. ECHA notes that no agrochemical uses have been identified for this substance in the technical dossier.

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, you are requested to carry out the following additional test using the registered substance subject to the present decision: Soil microorganisms: nitrogen transformation test, EU C.21/OECD TG 216.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposal(s) for examination pursuant to Article 40(1) on 26 April 2013.

ECHA held a third party consultation for the testing proposal(s) from 16 October 2014 until 1 December 2014. ECHA did not receive information from third parties.

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

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

You were notified that the draft decision does not take into account any updates after 6 July 2016, 30 calendar days after the end of the commenting period.

You updated your registration on 5 July 2016. ECHA took the information in the updated registration into account, and amended the draft decision. The updated information is reflected in the Reasons (Appendix 1).

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

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

Appendix 3: Further information, observations and technical guidance

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

2. Failure to comply with the 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.

3. In relation to the information required by the present decision, the sample of the substance used for the new test(s) must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants. It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new test(s) is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new test(s) 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 test(s) to be assessed.