ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 28 May 2019

Addressee: [redacted]

Decision number: TPE-D-2114471588-34-01/F
Substance name: Dodecamethylcyclohexasiloxane
EC number: 208-762-8
CAS number: 540-97-6
Registration number: [redacted]
Submission number: [redacted]
Submission date: 19/06/2018
Registered tonnage band: Over 1000

DECISION ON A TESTING PROPOSAL

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

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

1. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method OECD TG 443) in rats, oral route, with the registered substance, specified as follows:**
   - **Ten weeks premating exposure duration for the parental (P0) generation;**
   - **Dose level setting shall aim to induce systemic toxicity at the highest dose level;**
   - **Cohort 1A (Reproductive toxicity);**
     Cohort 1B (Reproductive toxicity) with extension to mate the Cohort 1B animals to produce the F2 generation;
   - **Cohorts 2A and 2B (Developmental neurotoxicity); and**
   - **Cohort 3 (Developmental immunotoxicity).**

While your originally proposed tests for 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 analogue substances decamethylcyclopentasiloxane (EC No 208-764-9; CAS RN 541-02-6) and octamethyltrisiloxane (EC No 203-497-4, CAS RN 107-51-7) are rejected, you are requested to perform:

2. **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.**
3. **Long-term toxicity on terrestrial invertebrates (Annex IX, Section 9.4.1. column 2, and Annex X, Section 9.4.4.); test method: Earthworm reproduction test, OECD TG 222 OR test method: Enchytraeid reproduction test, OECD TG 220, using the registered substance.**
4. **Long-term toxicity testing on plants (Annex IX, Section 9.4.3 column 2, and Annex X, Section 9.4.6.); test method: Terrestrial plants, growth test, OECD**

TG 208) OR test method: Soil Quality –Biological Methods – Chronic toxicity in higher plants, ISO 22030) using the registered substance.

You have to submit the requested information in an updated registration dossier by ***04 June 2021***. You also have to update the chemical safety report, where relevant.

The reasons for this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and 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, has to 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, Hazard Assessment

[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 you submitted and on scientific information submitted by third parties for the registered substance Dodecamethylcyclohexasiloxane, hereafter referred to as "target substance" or D6.

TOXICOLOGICAL INFORMATION

1. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

a) Examination of the testing proposal

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

The basic test design of an extended one-generation reproductive toxicity study (Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of 8.7.3., Annex X of the REACH Regulation. If the conditions described in column 2 of Annex X are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3. Further detailed guidance on study design and triggers is provided in the ECHA *Guidance on information requirements and chemical safety assessment,* Chapter R.7a, Section R.7.6 (version 6.0, July 2017) (below "the ECHA Guidance").

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 an extended one-generation reproductive toxicity study (EOGRTS) according to OECD TG 443 by the oral route in rats to be performed with the registered substance. You have provided the following justification and specification of the study design:
"*- Basic test design. No triggers for extension of cohorts 1B, 2A, 2B and 3 are foreseen therefore, are not proposed.*
- Premating exposure duration for parental (P0) animals: At least 2 weeks.
- Basis for dose level selection: A dose range-finding study will be performed. Dose levels will be based on the results from the dose range-finding study. [...]
- Termination time for F2: F2 generation will be terminated on PND 4."

Additionally you confirmed the "*Species: rat"* and "*Route of administration: oral:gavage*"

ECHA requested your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (extended one-generation reproductive toxicity study). ECHA notes that you provided your considerations concluding 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 design requires modifications to fulfil the information requirement of Annex X, Section 8.7.3. of the REACH Regulation. In particular, ECHA notes that there are triggers to expand the study design, namely by including the extension of Cohort 1B as well as Cohort 3. Furthermore, the premating exposure duration needs to be ten weeks. These modifications are further justified below.

Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement. Thus, an extended one-generation reproductive toxicity study according to columns 1 and 2 of Section 8.7.3., Annex X is required. The following refers to the specifications of this required study.

Premating exposure duration and dose-level setting

You proposed *"Premating exposure duration for parental (P0) animals: At least 2 weeks"*

To ensure that the study design adequately addresses the fertility endpoint, the duration of the premating exposure period and the selection of the highest dose level are key aspects to be considered. According to the ECHA Guidance, the starting point for deciding on the length of premating exposure period should be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required if there is no substance-specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA Guidance. In this specific case, ten weeks exposure duration is supported by the lipophilicity of the substance ($logK_{ow}$ = 8.87 at 23.6°C) to ensure that the steady state in parental animals has been reached before mating.

In your comments you agreed with the ten weeks premating exposure duration.

You proposed that *"Dose levels will be based on the results from the dose range-finding study."* ECHA agrees since the highest dose level shall aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

If there is no relevant data to be used for dose level setting, it is recommended that a range-finding study (or range finding studies) is performed and that its results are reported with the main study. This will support the justifications of the dose level selections and interpretation of the results.

Species and route selection

You proposed testing in rats. According to the test method OECD TG 443, the rat is the preferred species. On the basis of this default consideration, ECHA considers that testing should be performed in rats.

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) Chapter R.7a, Section 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.

Extension of Cohort 1B

If the column 2 conditions of 8.7.3., Annex X are met, Cohort 1B must be extended, which means that the F2 generation is produced by mating the Cohort 1B animals. This extension provides information also on the sexual function and fertility of the F1 animals.

You proposed that "*The study design will not include extension of Cohort 1B.*"

The use of the registered substance in the joint submission is leading to significant exposure of consumers and professionals because the registered substance is used by professionals in cosmetics and personal care products (leave-on products). The substance is also used by consumers in (i) personal care "wash off" products (e.g. bath oils, suntan and shaving products, and skin cleansing products, and hair care products such as conditioners) and "leave on" products (e.g. antiperspirants, skin creams and lotions), (ii) polishes and waxes, (iii) washing and cleaning products, (iv) pharmaceuticals, and (v) medical devices.

In addition, there are indications that the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure because the substance is lipophilic (Log K_{ow} = 8.87), and it meets the very bioaccumulative (vB) criteria.[2]

Therefore, ECHA concludes that Cohort 1B must be extended to include mating of the animals and production of the F2 generation because the uses of the registered substance are leading to significant exposure of professionals and consumers and the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure.

In your comments you agreed to extend Cohort 1B to produce the F2 generation.

Cohorts 2A and 2B

The developmental neurotoxicity Cohorts 2A and 2B need to be conducted in case of a particular concern on (developmental) neurotoxicity as described in column 2 of Section 8.7.3., Annex X. When there are triggers for developmental neurotoxicity, both the Cohorts 2A and 2B are to be conducted as they provide complementary information.

You proposed that no triggers for extension of cohorts 2A and 2B are foreseen.

ECHA notes that existing information on the registered substance itself derived from available *in vivo* studies (the OECD TG 422 study, "[redacted] 2005/KEY Repeated dose toxicity: oral 7.5.221") shows evidence of thyroid follicular cell hypertrophy at a dose level of 1000 mg/kg/day. Follicular cell hypertrophy is a sign of thyroid toxicity which indicates that there are changes in thyroid hormones. ECHA notes your consideration that this effect is " ... secondary and adaptive, and typical of a xenobiotic which induces hepatic microsomal enzymes with increased degradation of thyroxin and triiodothyronine as a side effect." ECHA considers that this consideration is speculative since the causal link between the liver effects and thyroid effects is unproven for this substance. Further, an aetiology of the thyroid effects is not by itself a basis for disregarding the follicular cell hypertrophy as a basis for triggering the extension of cohorts 2A and 2B.
ECHA also notes that there is another 28-day oral study on the registered substance {"A 28-day subchronic oral gavage feasibility study of various low molecular weight silicone oligomers in rats" (1990)}, but this study provides no relevant evidence in view of the lack of examination of thyroid tissue and other limitations of the study (e.g. insufficient control animals). There is also a 90-day inhalation study on the registered substance. This is a reliable study where the maximum dose appears to be limited by local effects (i.e. nasal effects) which are associated with inhalation exposure. The top dose is 546 mg/m^3, roughly

[2] Agreement of the Member State Committee on the identification of Dodecamethylcyclohexasiloxane (D6) as a substance of very high concern (https://echa.europa.eu/documents/10162/81c323a0-f0ce-8375-5091-b08d44f35553)

equivalent to an oral dose of 140 mg/kg/day. In view of the much higher dose that is given in the oral study (i.e. 1000 mg/kg/day oral, vs ~140 mg/kg/day inhalation), ECHA considers that the results of the inhalation 90-day study do not remove the concern for thyroid toxicity that is seen in the OECD TG 422 study.

ECHA concludes that the observed thyroid follicular cell hypertrophy is a sign of thyroid toxicity, which indicates that there are changes in thyroid hormones. Perturbation of thyroid hormone levels is a specific mechanism of action associated with developmental neurotoxicity. There is therefore a particular concern for developmental neurotoxicity justified by a specific mechanisms/modes of action of the substance with an association to developmental neurotoxicity.

ECHA concludes that the developmental neurotoxicity Cohorts 2A and 2B need to be conducted because there is a particular concern on (developmental) neurotoxicity based on the results from the above-identified *in vivo* study on the registered substance itself.

Cohort 3

The developmental immunotoxicity Cohort 3 needs to be conducted in case of a particular concern on (developmental) immunotoxicity as described in column 2 of Section 8.7.3., Annex X.

You proposed that "*The study design will not include Cohorts 3.*"

ECHA notes that existing information on a substance structurally analogous to the registered substance (octamethylcyclotetrasiloxane (D4), EC No 209-136-7) derived from the available two-generation reproductive toxicity study shows effects on the spleens of F1 animals: "*At the PND 28 necropsy of unselected weanlings, mean spleen weights were reduced in males in the 300, 500 and 700 pp groups and in females of the 500 and 700 ppm groups. These decreases were generally statistically significant and could have been related to exposure to D4.*" As the spleen weights were unaffected on PND 21, the substance seems to affect maturation of spleen in F1.

In your comments you disagreed with inclusion of Cohort 3 and considered that another structurally similar substance, decamethylcyclopentasiloxane (D5), would be structurally closer to the registered substance D6 than D4, and that the decrease seen in F1 animals' spleen weights in a two-generation reproductive toxicity study with D5 does not show apparent exposure-response relationship and therefore the decrease was not attributed to test article exposure. Finally, you concluded that the "*weight of evidence suggests that no developmental immunotoxicity is to be expected with the registered D6*", but you did not explain this approach any further.

ECHA-S agrees that D5 is structurally analogous to the registered substance but notes that the publicly available report on the two-generation study (30, 70 and 160 ppm) with D5 does not inform on effects in F1 animals' spleens and therefore ECHA cannot verify or confirm your analysis on exposure-response relationship or test article-related effects. However, ECHA-S notes that the two-generation reproductive toxicity study with the other analogue D4 (300, 500 and 700 ppm) shows effects in the spleens of F1 weanlings in all dose groups, as described above.

ECHA concludes that the developmental immunotoxicity Cohort 3 needs to be conducted because there is a particular concern on (developmental) immunotoxicity based on the results from the above-identified *in vivo* study on a substance structurally analogous to the registered substance.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation. For the reasons explained further below the information provided by third parties is not sufficient to fulfil this information requirement.

ECHA acknowledges that the third party has proposed a read-across approach for you to consider, using two structurally-related substances: octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5), as source substances, stating that "*Two-generation reproductive toxicity studies are available for D4 and D5 and should therefore be considered as source studies for read-across, based on the common metabolic pathway and the absence of systemic exposure to intact D6 following oral dosing.*"

ECHA notes that it is your responsibility to consider and justify any adaptation of the information requirements in accordance with the relevant conditions as established in Annex XI, Section 1.5. Therefore, you may assess whether you can justify a read-across as suggested by the third party.

However ECHA considers that the information as provided by the third party is insufficient for demonstrating that the conditions of Annex XI, Section 1.5. of the REACH Regulation are met. For example, the third party's proposal relies on "*common metabolic pathway and the absence of systemic exposure to intact D6 following oral dosing*" but he has neither provided any comparable toxicity data for the proposed source and target substances, nor justified the claim of absence of systemic exposure to intact D6. However from the toxicokinetic studies provided, ECHA notes that radioactivity of the parent D6 was detected in e.g. liver and bone marrow (in rat study), and in plasma samples (in rabbit study). Furthermore, the proposed source studies are not available in the registration dossier for the registered substance.

In addition, the third party provided his considerations on your proposed study design and stated that the basic study design (Cohorts 1A and 1B without extension) "*is considered to be appropriate in the absence of any triggers or conditions necessitating the inclusion of additional cohorts or a further generation*". However, the third party did not provide any scientific data which would fulfil this information requirement.

c) Outcome

Therefore, pursuant to Article 40(3)(b) of the REACH Regulation, you are requested to carry out the modified study with the registered substance subject to the present decision:

Extended one-generation reproductive toxicity study (test method OECD TG 443), in rats, by oral route, according to the following study-design specifications:
- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce systemic toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) with extension to mate the Cohort 1B animals to produce the F2 generation;
- Cohorts 2A and 2B (Developmental neurotoxicity); and
- Cohort 3 (Developmental immunotoxicity).

ECOTOXICOLOGICAL INFORMATION

You proposed a testing strategy intending to fulfil the standard information requirement for Effects on soil micro-organisms (Annex IX, Section 9.4.2.), by testing two analogue substances, namely Decamethylcyclopentasiloxane (hereafter referred to as source substance or D5) (EC No 208-764-9, CAS RN 541-02-6;) and octamethyltrisiloxane (hereafter referred to as source substance or L3) (EC No 203-497-4, CAS RN 107-51-7,).

The results from the structural analogues will then be used to adapt the standard information requirements by using read-across and grouping approach following Annex XI, Section 1.5. of the REACH Regulation.

ECHA has considered first the scientific validity of the proposed read-across and grouping approach (Section "Grouping of substances and read-across approach" below), before assessing the testing proposed (Section 2, below) and the testing additionally required (Sections 3 and 4 below).

Grouping of substances and read-across approach

a. Legal Background on ECHA's assessment of the grouping of substances and read-across hypothesis

The evaluation by ECHA of testing proposals submitted by registrants aims at ensuring that generation of information is tailored to real information needs. To this end, it is necessary to consider whether programmes of testing proposed by you are appropriate to fulfil the relevant information requirements and to guarantee the identification of health and environmental hazards of substances. In that respect, the REACH Regulation aims at promoting wherever possible the use of alternative means, where equivalent results to the prescribed test are provided on health and environmental hazards.

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated whenever possible by means other than vertebrate animal tests, including information from structurally related substances (grouping of substances and read-across), "*provided that the conditions set out in Annex XI are met*".

The first Recital and the first Article of the REACH Regulation establish the "*promotion of alternative methods for assessment of hazards of substances*" as an objective pursued by the Regulation. In accordance with that objective, ECHA considers whether a prediction of the relevant properties of the substance subject to the present decision by using the results of the proposed tests is plausible based on the information currently available.

b. Description of the proposed grouping and read-across approach

You have provided arguments to justify the read-across approaches only in general terms. You have also provided a Siloxane analogue report [redacted] as a separate attachment in IUCLID, Section 13
In your Siloxane analogue report, you identified that the target substance is "*within the analogue group of siloxanes (alkyl, vinyl, aryl or hydrogen substituted) (defined in the analogue overview report as sub-class I-3)*".

In the Siloxane analogue report you indicated that when choosing test substances for further terrestrial testing you have considered "1) *The quality of read-across between*

individual source and target read-across substances, in terms of: a. Chemical structure, b. Physicochemical (partitioning and degradation) properties; 2) The overall coverage of the category in terms of the parameters mentioned in point 1 and the quality of the overall data set. This is important both as a background to readacross justification and for validation of the equilibrium partitioning model; 3) Feasibility of testing (see Section 2.4.3.3.3 Testing method – technical challenges)".

You refined the read-across approach for the testing proposed in the CSR under the ecotoxicological endpoints and in the technical dossier under endpoint summary of Terrestrial toxicity as follows: "*This registration substance is a member of an analogue group of siloxanes. In view of the high potential to adsorb to soil and the potential persistence in soil for siloxane substances, and the lack of terrestrial toxicity testing across the analogue group, it is concluded that further testing is required. An integrated terrestrial toxicity testing strategy for the analogue group is proposed to validate the use of read-across (or equilibrium partitioning) within the analogue group. Reconsile plans to carry out stability tests, replicating the testing conditions of standard OECD studies, prior to conducting the OECD soil toxicity testing studies.".*

In the Siloxane analogue report you identified that two "*top priority*" substances to test are D5 "*for which several terrestrial toxicity studies are already available*", and L3 "*as a representative short-chain linear siloxane*". You also described the data gap filling approach for terrestrial compartment as: "*Due to the high adsorption potential of substances having a log Kow ≥8, read-across from D5 has been used in these instances. The behaviour of a substance in the environment and once ingested is considered to be dominated by the high log Kow. A substance is not expected to be readily desorbed from particles or to be readily taken up by organisms when the log Kow reaches values of 8 or more.*
For lower log Kow substances, EPM is thought to be sufficiently valid to conduct an interim risk characterisation, however in many cases the data used to derive a PNEC for soil based on EPM are limit values."

c. Information submitted to support the grouping and read-across approach

In ECHA's understanding, the Siloxane analogue report "*sets out the analogue methods applicable to linear/branched and cyclic siloxanes*",presents the substances within the analogue group of siloxanes (alkyl, vinyl, aryl or hydrogen substituted), and describes the existing data, intended analogue methods and proposed testing regarding physicochemical, degradation, bioaccumulation and ecotoxicological properties in pelagic, benthic and terrestrial compartments.

Apart from the above general information, in ECHA's understanding, you have provided general information on the testing strategy for environmental hazard assessment, in the technical dossier, under the endpoint summary for Terrestrial toxicity, in Section 6.3 and in the Chemical Safety Report (CSR) in section 7.0. This information includes description of the properties of substances in the class of siloxanes in general terms, followed by information regarding the read-across approaches proposed to be applied to terrestrial toxicity.

d. ECHA analysis of the grouping approach and read-across hypothesis in light of the requirements of Annex XI, Section 1.5.

ECHA notes that the registrants of siloxanes (alkyl, vinyl, aryl or hydrogen substituted) have grouped the substances in 'analogue group', including the substance subject to the current decision. Based on the substance specific justification for read-across approach provided by you for the registered substance, ECHA understands that no category hypothesis/

justification has been included and the proposed prediction is based on the analogue approach using decamethylcyclopentasiloxane (D5; CAS No 541-02-6) and octamethyltrisiloxane (L3; CAS No 107-51-7) as source substances.

According to ECHA's understanding you suggest that the proposed read-across and selection of test substances is based on similar physicochemical properties and on structural similarity.

In the following, ECHA examines whether the substances have indeed similar properties or that they would follow a regular pattern in their properties.

(i) Structural (dis)similarities and their impact on prediction

Structural similarity is a prerequisite for applying the grouping and read-across approach, but ECHA does not accept in general or this specific case that structural similarity *per se* is sufficient to enable the prediction of ecotoxicological properties of a substance, since structural similarity does not always lead to predictable or similar ecotoxicological properties. It has to be justified why such prediction is possible in view of the identified structural differences and the provided evidence has to support such explanation. In particular, the structural similarities must be linked to a scientific explanation of how and why a prediction is possible.

ECHA notes that you have not described whether you consider the target and source substances to be structurally similar. You note, in general, that you have considered the quality of read-across between individual source and target read-across substances, in terms of "*chemical structure*" and "*physicochemical (partitioning and degradation) properties*". You consider that D5 and L3 are a "*top priority*" substances to test because "*several toxicity studies are already available*".

Even though no description on potential structural similarity/dissimilarity is provided by you, ECHA notes the following. Both the target and source substance D5 are cyclic siloxanes and both are monoconstituents. Therefore the target and D5 are structurally similar. They differ from one another in chain length, only. On the contrary, L3 is an aliphatic siloxane and hence there is a clear structural difference between the target and L3. You provide no explanation on whether such structural difference would influence the predicted property.

You further intend to support the structural similarity in the Siloxane analogue report. You state that the choice of substances for testing is based on e.g., "*structural similarity, represented by the Tanimoto similarity index using an enhanced MDL fingerprint for the representation of Si-compounds*". ECHA acknowledges that molecular similarity indexes (e.g. the Tanimoto similarity index) can be considered when searching for relevant source chemicals for comparison. However, ECHA considers that such approaches give only an indication regarding potential similarity and do not provide a justification for the structural differences between the target and source substances and how they influence the property to be predicted.

ECHA notes that you have not provided any description on how the structural differences between the target and source substances may impact the toxicity of the substances and thus affect the possibility to predict properties of the target substance from the data obtained with the source substances.

(ii) Similar properties or regular pattern as a result of structural similarity

Annex XI, Section 1.5. provides that *"substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances"*. One prerequisite for a prediction based on read-across therefore is that the substances involved are structural similar and are likely to have similar properties. One important aspect in this regard is the analysis of the data matrix to compare the properties of source and target substances and to establish whether indeed they are similar or follow a regular pattern.

In your general read-across justification you state that you have considered the physicochemical properties when choosing the proposed source substances. However, you provide no discussion on the physico-chemical parameters/properties of the target and source substance specifically. You report in your attached analogue report the log Kow values (8.9 for D6, 8.0 for D5, 6.6 for L3), the log Koc values (5.17 for D5, 4.34 for L3), water solubility (0.0051 mg/L mg/L for D6, 0.017 mg/L for D5, 0.03449 mg/L for L3), and vapour pressure values (4.7 Pa for D6, 33.2 Pa for D5, 530 Pa for L3).

ECHA observes that there are differences in the physicochemcial properties between the target and source substances, which have impact on your hypothesis, for example, the Log Kow value for the target D6 is higher (8.9) than the logKow values of the source substances D5 (8.0) and L3 (6.6). ECHA notes that you define applicability boundaries for using read-across data from D5 by *"Due to the high adsorption potential of substances having a log Kow ≥8, read-across from D5 has been used in these instances"*. In light of your reasoning on the impact of Kow on toxicity, the proposed read-across from D5 to D6 falls within the boundary you defined (≥8). You justify the boundary of logKow of 8 by *"The behaviour of a substance in the environment and once ingested is considered to be dominated by the high log Kow. A substance is not expected to be readily desorbed from particles or to be readily taken up by organisms when the log Kow reaches values of 8 or more."*

ECHA acknowledges that the high logKow may indicate a high adsorption to particles. However, ECHA notes that you did not provide any evidence for this definition of the applicability boundary, nor to what extent the substances may be desorbed or taken up by organisms. On the contrary, ECHA notes that the sediment studies presented in the Siloxane analogue report indicate that even siloxanes such as D5 and D6, which have a logKow > 8 and which you thus do not expect to be readily desorbed and taken up by organisms, do actually exhibit toxicity in sediment organisms such as *Lumbriculus variegatus* and *Chironomus riparius* when tested in artificial sediments. Therefore, ECHA considers that the results of the sediment toxicity studies provide contradicting evidence to your arguments that highly adsorptive substances would not be taken up by organisms. As a consequence, further explanations and supporting evidence would be needed to justify the prediction possibility of terrestrial toxicity properties from D5 to the target substance D6. ECHA further notes that the logKow of the other proposed source substance L3 is below 8 and you do not justify how the properties of the target substance D6 can be predicted from the terrestrial toxicity data for L3.

Therefore, ECHA notes that you have not addressed how the different physicochemical properties of the substances will influence their stability in soil, bioavailability of the substances to the target organisms and thus their toxic potential in the time course of terrestrial toxicity testing, and in the terrestrial environment. ECHA notes that you have not adequately explained how the presented differences affect the prediction.

In your read-across justification you indicate that you have considered degradation properties when choosing the proposed source substances. However, ECHA notes that you provide no further discussion on the degradation properties of the target and source substance in soil and whether you consider them to be similar. Nevertheless ECHA notes that as the testing proposed concerns terrestrial environments and target and both source substances have potential to adsorb, their degradation potential in soil may be the most relevant property to address in assessing whether they have similar fate in the test media.

ECHA notes that in the technical dossier result for a D6 non-GLP soil simulation study is given, and according to the Siloxane analogue report similar soil degradation data is available for the source substances D5 and L3. The half-life for D6 are reported to be 1.38d in Wahiawa soil (32% relative humidity), whereas for D5 a half-life of 0.08 day is reported for the same soil and same relative humidity. For L3 a half-life of 0.26 d is reported for relative humidity of 32% in Loamy silt soil. The transformation products are identified to be "*Siloxane diols*" and "*Dimethylsilanediol*" for D5 and D6. For L3 you report transformation products "*Dimethylsilanediol*", "*Trimethylsilanol*" and "*3,3,3,1,1-Pentamethyldisiloxanol*", and are thus partly different than for the target substance D6.

ECHA notes that there are uncertainties related to the reporting and reliability of these studies. It is, for example, not clear from the justification document whether the reported half-lives refer to the first step of transformation or to the ultimate degradation of the substances. Also the information given on metabolites is not specific enough and no further evaluation of the fate of the degradation products is provided. ECHA considers it not possible to reach a conclusion on whether degradation between the target and source substances are similar. Based on the information provided it is also not possible to verify to what degree the organisms would be exposed to the target and source substances during toxicity testing, and to what degree they would be exposed to any potential (unidentified) degradation products.

In summary, ECHA considers that you have not provided adequate and relevant information on the degradation of the target and source substances. ECHA notes that you have not explained how the potential differences in degradation will influence the substances' stability in soil, production and impact of degradation products, and how the potential differences in degradation affect the prediction.

Finally, ECHA notes that in your justification you have not considered the ecotoxic potential of target and source substances in terrestrial compartment. ECHA notes that in the Siloxane analogue report you provide results on D5, but no terrestrial toxicity data is provided for L3 or the target substance D6. Hence, there are no data to support the similarity in terrestrial toxicity between the target and the source substances.

Indeed, as discussed above, the pysicochemical and degradation properties of the target and source substances are different, which may be reflected in differences in toxic potential. ECHA considers that you did not demonstrate similarity in bioavailability and bioaccumulation properties among the substances (and their degradation products), and did not address how the potential differences in these properties do not influence the toxic potential of the substances in terrestrial environments.

In summary, ECHA concludes that based on the presented information it is not possible to confirm that the substances would have similar properties or they would follow a regular pattern in their properties regarding terrestrial toxicity. In the absence of such information

there is not an adequate basis for predicting the properties of the target substance from the data obtained with the source substance.

e. Conclusion on the read-across approach

Based on the above considerations ECHA concludes that you have not provided adequate and reliable information to demonstrate that the proposed read-across approach is plausible for the environmental endpoint(s) in consideration.

ECHA therefore concludes that the criteria of Annex XI, Section 1.5, are not met, and consequently the testing proposed on the read-across substance(s) is not appropriate to fulfil the information requirement(s)of the substance subject to the present decision.

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

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.

"Effects on terrestrial organisms" is a standard information requirement as laid down in Annex IX and Annex X, Section 9.4. of the REACH Regulation. The Registrant must address the standard information requirements set out in Annex IX and X, Section 9.4., for different taxonomic groups: short-term or long-term toxicity testing on invertebrates (Annex IX Section 9.4.1., Annex X Section 9.4.4), effects on soil micro-organisms (Annex IX, Section 9.4.2.), and short-term or long-term toxicity testing on plants (Annex IX Section 9.4.3., Annex X Section 9.4.6).

The information on "effects on soil micro-organisms" 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 the same testing proposal, for each of the following two analogue substances: decamethylcyclopentasiloxane (D5), and octamethyltrisiloxane (L3), to study the effects on soil micro-organisms (Soil Microorganisms: Nitrogen Transformation Test, OECD TG 216).

ECHA has evaluated your proposal to test the analogue substances. As explained above, the proposed read-across cannot be accepted. Hence there is a need to test the registered substance.

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 2.0, November 2014), ECHA considers the nitrogen transformation test (EU C.21/OECD TG 216) suitable for non-agrochemicals. Therefore, the proposed test *Soil Microorganisms: Nitrogen Transformation Test*, OECD TG 216 is suitable to address the information requirement of Annex IX, Section 9.4.2.

In your comments on the terrestrial testing requirements (requests 2 to 4) you indicated that as the substance has been "*included into the Candidate List of substances of very high*

concern (ECHA's decision of 20 June 2018, effective 27 June 2018), we are concerned that carrying out the additional tests to determine hazards in the terrestrial compartment will not lead to additional information that facilitates risk management."

In response ECHA observes the following.

First, section 9.4, second column of Annexes IX and X of REACH provides that studies examining the effects of terrestrial organisms do not need to be conducted if exposure of the soil compartment is unlikely.

Second, Annex I, point 6.5 provides that for "*substances satisfying the PBT and vPvB criteria, the manufacturer or importer shall use the information as obtained in Section 5, Step 2 when implementing on its site, and recommending for downstream users, risk management measures which minimise exposures and emissions to humans and the environment, throughout the lifecycle of the substance that results from manufacture or identified uses".*

Third, and consequently, the information requirements for terrestrial toxicity can be waived under section 9.4 second column for substances satisfying the PBT/ vPvB criteria if the registrant indicates that it has in accordance with Annex I, point 6.5., introduced measures to minimise exposures and emissions to humans and the environment.

ECHA notes that the substance satisfies the PBT/ vPvB criteria following ECHA's decision of 20 June 2018 to which you refer. However, you have not updated your registration dossier to reflect that the substance is PBT/ vPvB. In addition, your technical dossier does not indicate that risk management measures have been introduced to minimise exposure to the substance. Finally, your technical dossier does not contain an adaptation in accordance with section 9.4. second column of Annexes IX and X indicating that exposure to the soil compartment is unlikely as a result of the risk management measures taken in consequence of ECHA's decision identifying the substance as a PBT/ vPvB substance.

ECHA therefore considers that as long as the consequences of the PBT/vPvB status of your substance is not properly reflected in your dossier, there is a data gap. Accordingly, based on the current information in your technical dossier it is necessary to submit the data requested.

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, you are requested to carry out the following test using the registered substance: Soil microorganisms: nitrogen transformation test, EU C.21/OECD TG 216, while your originally proposed tests for Soil microorganisms: nitrogen transformation test (OECD TG 216) using the analogue substances decamethylcyclopentasiloxane (D5; CAS RN 541-02-6) and octamethyltrisiloxane (L3, CAS RN 107-51-7) are rejected according to Article 40(3)(d) of the REACH Regulation.

3. Long-term toxicity to terrestrial invertebrates (Annex IX, Section 9.4.1., column 2, and Annex X, Section 9.4.4.)

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.

"Effects on terrestrial organisms" is a standard information requirement as laid down in Annex IX and Annex X, Section 9.4. of the REACH Regulation. The Registrant must address the standard information requirements set out in Annex IX and X, Section 9.4., for different taxonomic groups: short-term or long-term toxicity testing on invertebrates (Annex IX Section 9.4.1., Annex X Section 9.4.4), effects on soil micro-organisms (Annex IX, Section 9.4.2.), and short-term or long-term toxicity testing on plants (Annex IX Section 9.4.3., Annex X Section 9.4.6). Column 2 of Annex IX, Section 9.4 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} 8.9). Therefore ECHA considers that long-term testing on terrestrial invertebrates is a standard information requirement for your registration dossier, in accordance with Annex IX, Section 9.4.1. column 2, and Annex X, Section 9.4.4.

You have submitted two long-term terrestrial toxicity studies on an analogue substance decamethylcyclopentasiloxane (D5; CAS RN 541-02-6): one study was conducted according to Environment Canada (EPS 1/RM/43, June 2004) with *Eisenia andrei*, and another according to Environment Canada (1/RM/47, June 2007) with *Folsomia candida*. ECHA notes that as explained above, the proposed read-across from D5 to the registered substance in the information requirement on toxicity to soil micro-organisms is rejected. The read-across proposed for this information requirement is likewise not accepted for the same reasons as described above.

Consequently there is an information gap and it is necessary to provide information for this endpoint.

The test requested by ECHA under request 2 above is not sufficient by itself to address the standard information requirements of Annex IX, section 9.4.1. and Annex X, section 9.4.4. ECHA notes that the registration dossier does not contain data for this endpoint.

Please refer to request 2 above for ECHA's reply to your comments on the terrestrial testing requests. In summary, ECHA considers that as long as the consequences of the PBT/vPvB status of your substance is not properly reflected in your dossier, there is a data gap. Accordingly, based on the current information in your technical dossier it is necessary to submit the data requested.

The earthworm reproduction test (OECD TG 222), Enchytraeid reproduction test (OECD TG 220), and Collembolan reproduction test (OECD TG 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. You are to apply the most appropriate and suitable test guideline among those listed above. However ECHA notes that when log K_{ow} >5 and log K_{oc} >4, as in this case, the test OECD TG 232 is not appropriate as the dominant route of exposure for Collembolans is via pore water.
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:

Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*) OECD TG 222, or Enchytraeid reproduction test, OECD TG 220.

4. Long-term toxicity to terrestrial plants (Annex IX, Section 9.4.3. column 2, and Annex X, Section 9.4.6.)

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.

"Effects on terrestrial organisms" is a standard information requirement as laid down in Annex IX and Annex X, Section 9.4. of the REACH Regulation. The Registrant must address the standard information requirements set out in Annex IX and X, Section 9.4., for different taxonomic groups: short-term or long-term toxicity testing on invertebrates (Annex IX Section 9.4.1., Annex X Section 9.4.4), effects on soil micro-organisms (Annex IX, Section 9.4.2.), and short-term or long-term toxicity testing on plants (Annex IX Section 9.4.3., Annex X Section 9.4.6). Column 2 of Annex IX, Section 9.4 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} 8.9). Therefore ECHA considers that long-term testing on terrestrial plants is a standard information requirement for your registration dossier, in accordance with Annex IX, Section 9.4.3. column 2, and Annex X, Section 9.4.6.

The test requested by ECHA under request 2 above is not sufficient by itself to address the standard information requirements of Annex IX, Section 9.4.3. and Annex X, Section 9.4.6.

You have submitted a study for short-term toxicity to plants on the analogue substance Decamethylcyclopentasiloxane (D5). In the endpoint summary you state that "*There are no data describing the long-term toxicity of the registered substance to terrestrial plants. However, data are available for the siloxane decamethylcyclopentasiloxane (D5, CAS: 541-02-6). A 14-day IC50 value of 209 mg/kg dry weight has been determined for the effects of the test substance on root dry mass of Hordeum vulgare. IC50/EC50 values for effects on seedling emergence, root and shoot length and shoot dry mass determined in the same test were ≥ 248 mg/kg dry weight. 14-day EC50 values of >4054 mg/kg dry weight have been determined for the effects of the test substance on seedling emergence, root and shoot length and root and shoot dry mass of Trifolium pratense. NOECs were not determined in the tests. The read-across is considered to be reliability 2".*

ECHA notes that, as explained above, the proposed read-across from D5 to the registered substance for the information requirement of toxicity to soil micro-organisms is rejected. The read-across proposed for this information requirement is likewise not justified for the same reasons as described above.

Moreover, ECHA considers that the study submitted cannot be considered sufficient to fulfil the information requirement of long-term toxicity testing on plants, as it does not have adequate and reliable coverage of the key parameters addressed in the corresponding test method and the exposure duration is not comparable, as required by Annex XI, Section 1.5.

of the REACH Regulation. ECHA notes that only two species were studied over 14 days, and the endpoint studied were number of emerged seedlings, shoot and root length and dry biomass. In the test guideline designed to assess long-term toxicity to plants, e.g. OECD TG 208, effects on six plant species are studied until 14 to 21 days after 50 % of the control plants have emerged. The study you have submitted does not provide the information for six species and the study duration is shorter.

In addition to the short-term study submitted, you have proposed to adapt this standard information requirement by the following: *"In accordance with Column 2 of REACH Annex X, long-term toxicity testing with terrestrial plants (required in Section 9.4.5 of REACH Annex X) does not need to be conducted as the chemical safety assessment according to Annex I indicates that this is not necessary."*

However, the adaptation cannot be accepted because all terrestrial toxicity data you have provided are for the analogue substance D5. As explained above, the proposed read-across from D5 to the registered substance for the information requirement of toxicity to soil micro-organisms is rejected. The read-across proposed for all terrestrial toxicity information requirements is likewise not justified for the same reasons as described above. In absence of any terrestrial toxicity data your claim of no indication of a need to conduct long-term toxicity testing is unjustified.

In conclusion, your justification for waiving does not meet the criteria of either the specific adaptation rules of Column 2 of Annexes IX and X, Section 9.4, or the general adaptation rules of Annex XI. Therefore, the adaptation cannot be accepted.

Consequently there is an information gap and it is necessary to provide information for the standard information requirements of Annex IX, Section 9.4.3 and Annex X, Section 9.4.6.

OECD TG 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. You should consider if testing on additional species is required to cover the information requirement.

Please refer to request 2 above for ECHA's reply to your comments on the terrestrial testing requests. In summary, ECHA considers that as long as the consequences of the PBT/vPvB status of your substance is not properly reflected in your dossier, there is a data gap. Accordingly, based on the current information in your technical dossier it is necessary to submit the data requested.

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 TG 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).

Notes for your consideration with regards to requests 3 and 4

Due to absence of chronic or long-term effects in aquatic organisms up to the substance solubility limit you have considered that it is unfeasible, with the currently available information, to derive a PNEC for aquatic organisms. Consequently, the Equilibrium

Partitioning Method (EPM) is not applicable in this case and it is not possible to allocate the substance to a soil hazard category (Section R.7.11.6., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, June 2017)). However, the abovementioned guidance document advocates that absence of aquatic toxicity can be used as part of a *Weight-of-Evidence* argument to modify/waive the data requirements of Annex IX and X and a single soil test on a suitable species would be adequate to meet the requirements of Annex IX/X. Where the substance is highly adsorptive (log K_{ow}/K_{oc} >5), and/or the substance is very persistent in soil, this single test should be a long-term test.

ECHA hence considers that you may start testing by performing one of the long-term terrestrial toxicity tests, the long-term toxicity to invertebrates or the long-term toxicity to plants test. Once the results of the first long-term terrestrial toxicity test are available, you should consider whether there is a need to investigate further the effects on terrestrial organisms in order to fulfil the information requirements of section 9.4 of Annex IX/X, and if necessary, to carry out the other long-term terrestrial study requested above. If you conclude that no further investigation of effects on terrestrial organisms is required, you should update your technical dossier by clearly stating the reasons for adapting the information requirements of Annex IX/X, Section 9.4. of the REACH Regulation.

ECHA emphasises that the intrinsic properties of soil microbial communities are not addressed through the aquatic data on invertebrates and/or fish and an adaptation provided for invertebrates/ plants may not be applicable for the information requirement of Annex IX, Section 9.4.2.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposals for examination in accordance with Article 40(1) on 4 January 2018.

ECHA held a third party consultation for the testing proposals from 23 April 2018 until 7 June 2018. ECHA received information from third parties (see Appendix 1).

This decision does not take into account any updates after **7 November 2018**, 30 calendar days after the end of the commenting period.

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

ECHA took into account your comments and did not amend the requests.

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

ECHA received proposal(s) for amendment and modified the draft decision.

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

ECHA referred the draft decision to the Member State Committee.

You did not provide any comments on the proposed amendment(s).

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-64 written procedure and ECHA took the decision according to Article 51(6) 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 requests in this decision, or to otherwise fulfil the information requirements 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 tests 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 tests 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 tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.