SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Decamethyltetrasiloxane (L4)

EC No 205-491-7

CAS RN 141-62-8

Evaluating Member State(s): Norway, handover from United Kingdom

Dated: December 2021

Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2015

Before concluding the substance evaluation a Decision to request further information was issued on: 27. March 2017

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the Registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory risk management measures which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

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Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

The Substance, decamethyltetrasiloxane (L4) was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB
- Wide dispersive use;
- Consumer use

During the evaluation no additional concern was identified.

The assessment was targeted to the environmental concerns. However an evaluation of the information available for human health hazard endpoints relevant to the “T” criteria was made.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

A decision on testing proposal was adopted by ECHA in 2018, where the following tests were required:
1. Pre-natal developmental toxicity study in rats
2. Effects on soil microorganisms
3. Long-term toxicity on terrestrial invertebrates
4. Long-term toxicity testing on plants

Decamethyltetrasiloxane (L4) is part of a group of related linear siloxanes that are subject to substance evaluation for similar concerns. The linear siloxanes are suspected PBT/vPvB substances. The other substances in this group are hexamethyldisiloxane (L2), octamethyltrisiloxane (L3) and dodecamethylpentasiloxane (L5).

Data from these substances and the cyclic siloxanes octamethylcyclotetrasiloxane (D4), decamethylcyclopentasiloxane (D5) and dodecamethylcyclohexasiloxane (D6) have been used by the Registrant(s) to support their registrations and the eMSCA in their evaluation:

- SVHC on the basis of the criteria in REACH Articles 57(d) and 57(e) (PBT/vPvB): D4, D5 and D6 have been identified as SVHC (ECHA, 2015, 2018b).
- Restriction in wash-off cosmetic products for D4 and D5 entered into force by 31 January 2020, (ECHA, 2016).
- Restriction in leave-on personal care products and other consumer/ professional products is under consideration for D4, D5 and D6. Furthermore, a restriction of D6 in wash off and rinse off cosmetic products is included in the same restriction proposal (ECHA, 2020).

Some uses of the cyclosiloxanes are already or are in the process of being restricted in consumer products and in most professional uses under REACH. However, some of their uses (industrial production of electronics and some professional uses such as dry cleaning in closed systems) are not covered by these restrictions. These uses are in the process of being included into the authorisation list and companies will need to apply for authorisation to continue using them.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the substance has led the evaluating Member State to the following conclusions, as summarised in the table below.

Table 1

CONCLUSION OF SUBSTANCE EVALUATION	
Conclusions	**Tick box**
Need for follow-up regulatory action at EU level	X
Harmonised Classification and Labelling	
Identification as SVHC (authorisation)	X
Restrictions	X
Other EU-wide measures	
No need for regulatory follow-up action at EU level	

4. FOLLOW-UP AT EU LEVEL

4.1. Need for follow-up regulatory action at EU level

4.1.1. Harmonised Classification and Labelling

Not applicable.

4.1.2. Identification as a substance of very high concern, SVHC (first step towards authorisation)

L4 is considered to meet the criteria for very persistent and very bioaccumulative (vPvB) substances according to REACH 57(e) and Annex XIII.

This conclusion is based on read-across to test results available on sediment simulation testing of hexamethyldisiloxane (L2) and octamethyltrisiloxane (L3) and bioaccumulation data on L4 itself.

According to REACH (Annex I), exposure and emissions of PBT/vPvB substances should be minimized throughout the lifecycle of the substance. A first step would be the identification of L4 as a SVHC. In addition to leading to a formal recognition of the vPvB properties, Candidate Listing of L4 will also imply other legal obligations.
Suppliers of substances and mixtures containing L4 have to provide a safety data sheet to their customers. Furthermore, suppliers of articles are obliged to pass on information on the respective substances in the supply chain and upon request provide information to consumers. Producers or importers of articles have to notify ECHA if their article contains a substance being on the Candidate List. The formal recognition of L4 as a vPvB substance with the subsequent obligations for the supply chain is expected to result in emission reductions of L4.

4.1.3. Restriction

L4 is used by consumers and professional workers mainly in washing/cleaning products and cosmetics and personal care products. This wide dispersive use represents a significant potential for environmental releases.

The eMSCA concludes that L4 meets the vPvB criteria of REACH Annex XIII. Therefore, all emissions and environmental releases of L4 should be reduced as much as possible.

To avoid regrettable substitution, L4 should be restricted, since the substance has been identified as a potential alternative in the restriction of D4 and D5 in "wash-off cosmetic products" (ECHA, 2016).

4.1.4. Other EU-wide regulatory risk management measures

Not applicable.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1. No need for regulatory follow-up at EU level

Not applicable.

5.2. Other actions

Not applicable.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

Indication of a tentative plan is not a formal commitment by the evaluating Member State. A commitment to prepare a REACH Annex XV dossier (SVHC, restrictions) and/or CLP Annex VI dossier should be made via the Registry of Intentions.

Table 2

FOLLOW-UP		
Follow-up action	**Date for intention**	**Actor**
Identification as SVHC (authorisation)	-	Not agreed yet
Restriction	-	Not agreed yet
RMOA	-	Not agreed yet

The option of including L4 in other EU-wide regulatory risk management measures will be assessed in the RMOA for the group of linear siloxanes L2, L3, L4 and L5, due to PBT/vPvB concern.

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

The Substance, decamethyltetrasiloxane (L4) was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB
- Wide dispersive use;
- Consumer use

During the evaluation no additional concern was identified.

The assessment was targeted to the environmental concerns. However an evaluation of the information available for human health hazard endpoints relevant to the “T” criteria was made.

Table 3 shows a list of evaluated endpoints with the corresponding outcomes. More details can be found in the relevant sections below.

Table 3

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome / conclusion**
Persistence	Concern confirmed. Conclude substance as vP based on read-across to currently available information on sediment simulation testing OECD TG 308 for L3 and L2.
Bioaccumulation	Concern confirmed. Conclude substance is vB based on currently available information on bioaccumulation studies OECD TG 305 for L4.
Toxicity	Concern refuted. Conclude L4 is not T based on currently available information on human and ecotoxicological studies.
Suspected vPvB properties	Concern confirmed. Conclude L4 is vPvB as explained above.
Exposure of environment and wide dispersive use	Concern confirmed. Based on use pattern there is wide dispersive use and exposure of the environment.

7.2. Procedure

Decamethyltetrasiloxane (L4) was included in the Community rolling action plan (CoRAP) for substance evaluation to be performed in 2015.

The initial assessment was initiated on 17 March 2015 by the UK as eMSCA. Due to the UK's departure from the EU on 31 January 2020, Norway took over the substance evaluation of L4 in the conclusion stage. The evaluation of the available test results relies mainly on the UKs assessment. Based on this, regulatory actions have been proposed by the Norwegian eMSCA.

Decamethyltetrasiloxane (L4) belongs to a group of related linear siloxanes that are subject to substance evaluation for similar concerns; that they could be PBT/vPvB substances. The related linear siloxanes are hexamethyldisiloxane (L2), octamethyltrisiloxane (L3) and dodecamethylpentasiloxane (L5). Data from these substances and from the cyclic siloxanes D4, D5 and D6 (octamethylcyclotetrasiloxane; decamethylcyclopentasiloxane, and dodecamethylcyclohexasiloxane) have been used by the Registrant(s) to support their registrations and have also been used by the eMSCA in their evaluation

Based on the evaluation of the available information, the eMSCA concluded that some uncertainty on the degradation of the registered substance and on exposure assessment and risk characterisation for the environment remained.

Therefore, it was necessary to request new data and a decision was endorsed by ECHA on 27 March 2017:

1) 1)Sediment simulation testing; test method: Aerobic and anaerobic transformation in aquatic sediment systems, EU C.24./ OECD TG 308, including the identification of transformation products, at a temperature of 12 °C;
2) OECD TG 218 Sediment-Water Chironomid Toxicity Test Using Spiked Sediment;
3) OECD TG 225 Sediment-Water Lumbriculus Toxicity Test Using Spiked Sediment;

   Tests 1, 2 and 3 should be carried out as a tiered testing strategy: Test 2 is required unless the outcome of test 1 is that the substance is vP; If test 2 is required, test 3 is also required unless the outcome of test 2 indicates the substance is T.
   For toxicity tests 2 and 3 above you shall measure the test substance concentration in the sediment, porewater and overlying water. All food shall be added to the sediment prior to the commencement of the tests.

4) Exposure assessment and risk characterisation for environment:
   Provide further information and justification on the input parameters used for the exposure assessment for ES3: Professional & consumer use of personal care products or, alternatively, provide separate scenarios for professional consumer use and household consumer use of personal care products, including clear justification of the environmental emission factors chosen for each.

On 13 February 2019, the Registrant(s) provided a final study report for the OECD TG 308 sediment simulation study for L2. A dossier update containing the requested information on degradation and exposure information for L4 was received on 25 June 2019 and thereafter the UK eMSCA considered the dossier as completed.

On 9 February 2021, the Registrant(s) provided a final study report for the OECD TG 308 sediment simulation study for L3 and the updated registration has been published at ECHA's disseminated page on 8 June 2021.

7.3. Identity of the substance

Table 4 displays the identity of the substance according to the ECHA dissemination website.

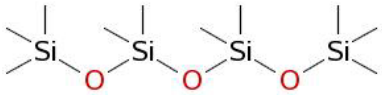
Table 4

SUBSTANCE IDENTITY	
Public name:	Decamethyltetrasiloxane
EC number:	205-491-7
CAS number:	141-62-8
Index number in Annex VI of the CLP Regulation:	n/a

Molecular formula:	$C_{10}H_{30}O_3Si_4$
Molecular weight range:	310.69
Synonyms:	L4, MD2M

Type of substance ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

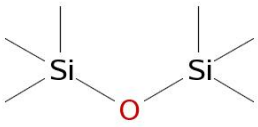
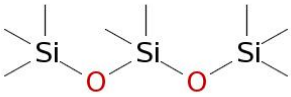
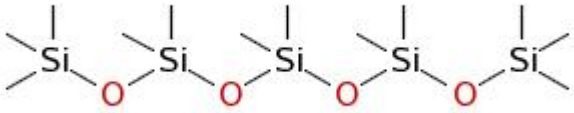
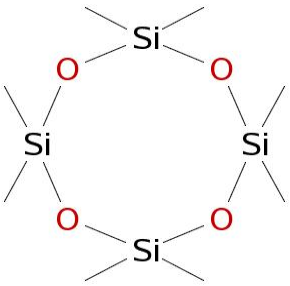
Structural formula:

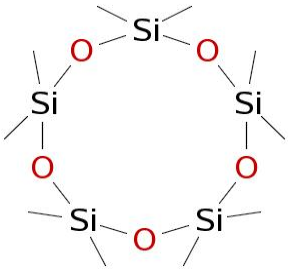
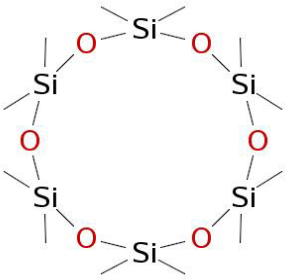


Category information

The following additional substances shown in Table 5 are relevant to consider in the assessment.

Table 5

Chemical	Structure
L2, hexamethyldisiloxane EC No. 203-492-7 CAS RN 107-46-0	
L3, octamethyltrisiloxane EC No. 203-497-4 CAS RN 107-51-7	
L5, dodecamethylpentasiloxane EC No. 205-492-2 CAS RN 141-63-9	
D4, octamethylcyclotetrasiloxane EC No. 209-136-7 CAS RN 556-67-2	

D5, decamethylcyclopentasiloxane EC no. 208-764-9 CAS RN 541-02-6	
D6, dodecamethylcyclohexasiloxane EC No. 208-762-8 CAS RN 540-97-6	

Appendix I to this report details the expected trends in PBT/vPvB properties across this group.

7.4. Physico-chemical properties

Table 6 displays the physicochemical properties of the substance according to information on the ECHA dissemination website.

Table 6

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	Colourless liquid
Melting/freezing point	-70 °C Publication
Boiling Point	194 °C Publication
Vapour pressure	73 Pa at 25°C Publication (Vapour pressure curve)
Water solubility	0.0067 mg/l at 23°C Publication (non-guideline. A non-colloidal, saturated solution prepared by slow-stirring and analysed by GC-MS)
Partition coefficient n-octanol/water (Log Kow)	8.21 at 25.1°C OECD 123 (Slow-stirring method)
Partition coefficient n-octanol-air (Log Koa)	4.87 ± 0.04 at 19.7 ±0.4°C
Flash Point	62-63 °C at 101.3 kPa Closed cup
Explosive properties	Data waiving
Oxidising properties	Data waiving
Stability in organic solvents and identity of relevant degradation products	Data waiving

Dissociation constant	Waiver - No ionisable groups
Relative density	0.85 at 25°C Publication
Auto Flammability	350°C at 101.3 kPa
Surface tension	Data waiving

7.5. Manufacture and uses

7.5.1. Quantities

Table 7 displays information from the ECHA dissemination website.

Table 7

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☐ 10 – 100 t	☒ 100 – 1000 t	☐ 1000- 10,000 t	☐ 10,000-50,000 t
☐ 50,000 – 100,000 t	☐ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☐ > 1000,000 t	☐ Confidential

7.5.2. Overview of uses

Table 8 lists the different uses stated for L4 on the ECHA's dissemination website.

Table 8

USES	Use(s)
Uses as intermediate	Not listed
Formulation	o Manufacturing and on-site use o Formulation at production sites o Cosmetics, personal care products o Non-metal-surface treatment products o Lubricants, greases, release products o Automotive care products
Uses at industrial sites	o Washing and cleaning products (including solvent based products) o Non-metal-surface treatment products o Lubricants, greases, release products o Laboratory use o Use in electronics and semi- conductors manufacturing o Use in electronics and optical product manufacturing o Heat transfer fluid
Uses by professional workers	o Laboratory chemicals o Cosmetics, personal care products o Automotive care products
Consumer Uses	o Cosmetics, personal care products o Automotive care products
Article service life	Not listed

Automotive care products for professional and consumer use have been registered as a new use area. This new use area leads to increased wide dispersal use, professional worker and consumer uses and an increased potential for environmental releases. A restriction on D4 and D5 in wash-off cosmetic products has been adopted, and a further restriction on D4, D5 and D6 for leave on personal care products and other consumer/professional products is in progress. L4 is an alternative replacement for the restricted uses of D4 and D5 in cosmetic products and the supply volume of L4 might increase in the future (ECHA, 2016).

Talalay (2007) and Triest and Alemany (2014) show the possible use of silicone fluids which are linear polydimethylsiloxane (PDMS) for ice core drilling. This PDMS can include L3, L4 and L5. The use for ice-drilling may provide a source of L3 in what would normally be considered remote areas. Triest and Alemany (2014) furthermore note that L3 and L4 are sold as anti-foam additives for oil drilling. The aforementioned use areas do not appear to be covered by the uses listed in the current registrations. This either means that the use area is not relevant in Europe, that it occurs at a tonnage below the current registration trigger, or that it was not realised commercially.

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

Not included in Annex VI of the CLP regulation.

7.6.2. Self-classification

Table 9

Number of notifiers	Self-classification
45 (December 2021)	H226: Flammable liquid and vapour.
124 (December 2021)	Not classified
25 (December 2021)	H413: May cause long lasting harmful effects to aquatic life.
13 (December 2021)	H226: Flammable liquid and vapour. H413: May cause long lasting harmful effects to aquatic life.

7.7. Environmental fate properties

7.7.1. Degradation

7.7.1.1. Abiotic degradation

7.7.1.1.1. Hydrolysis

The registration dossier contains a summary of a hydrolysis study conducted according to OECD Guideline 111, hydrolysis as a function of pH (registration dossier, 2009). The study is given a reliability - score of 1. Radiolabelled substance was used, as the concentration tested was low (3 µg/l, around half of the solubility). Precautions were taken to minimise volatilisation in the experiment (sealed test vessels) and the calculation methods used to obtain rate constants were adapted in some cases to allow for substance present in the headspace.

Low recoveries were seen in some of the experiments, 76-90% for the pH 5 and pH 9 studies and 55-70% for the pH 7 studies. These were attributed to losses during the preparation of the reaction tubes, and losses to the headspace in the case of the pH 7 studies.

The half-lives obtained from the study are presented in Table 10. These are for the disappearance of the parent substance.

Table 10: Hydrolysis half-life for L4

pH	Temperature (°C)	Half-life (hours)	Equivalent first order rate constant k_{obs} (day^{-1})
5	10	44.4 (1.9 days)	0.37
	25	14.0	1.19
	35	6.4	2.62
7	10	3,960 **(165 days)**	0.0042
	25	728 (30.3 days)	0.0228
	35	219 (9.1 days)	0.0761
9	10	180 (7.5 days)	0.0926
	25	21.1	0.789
	35	7.3	2.28

The initial products of hydrolysis are also unstable in water. The ultimate products of hydrolysis were dimethylsilanediol (detected) and trimethylsilanol (inferred, not detected due to the position of the radiolabel in the parent substance).
As can be seen from Table 10, the half-life for hydrolysis depends on the temperature and the pH.

The half-life at pH 7 and 10°C is around 165 days. The default environmental temperature assumed in the REACH guidance is typically 12°C for the freshwater environment and 9°C for the marine environment. However, the pH for the marine environment is generally higher (typically around pH 8).
Although not carried out in the registration dossier, it is possible to estimate the approximate hydrolysis half-life for the substance at 12°C and pH 7 and 9°C and pH 8 from the available data using the following approach.

At any given pH the observed first order rate constant (k_{obs}) determined in the study can be expressed in terms of the following equation.

$$k_{obs} = k_0 + k_{H3O+}[H_3O^+] + k_{OH^-}[OH^-] + k_a[acid] + k_b[base]$$

where:
k_0 = first order rate constant for the uncatalyzed reaction.
k_{H3O+} = second order rate constant for catalysis by hydronium ions.
$[H_3O^+]$ = concentration of hydronium ions.
k_{OH-} = second order rate constant for catalysis by hydroxide ions.
$[OH^-]$ = concentration of hydroxide ions.
k_a = second order rate constant for catalysis by/reaction with general acids.
[acid] = concentration of acid.
k_b = second order rate constant for catalysis by/reaction with general bases.
[base] = concentration of base.

Assuming that under the conditions of the test, a) general acid or base catalysis was not occurring and b) at pH 5 and pH 9 the rate of the uncatalyzed reaction was negligible compared with the rates catalysis by hydronium (pH 5) and hydroxide (pH 9) ions, the values of $k_{H30}+$ and $k_{[OH-]}$ can be estimated directly from the k_{obs} value measured at pH 5 (here $[H_3O^+] = 1\times10^{-5}$ mole/l) and pH 9 (here $[OH^-] = 1\times10^{-5}$ mole/l). Thus k_{H3O+} = 119,000 l $mole^{-1}$ d^{-1} and k_{OH-} = 78,900 l $mole^{-1}$ d^{-1}, both at 25°C.

At pH 7, $k_{obs} = k_0 + (119{,}000\times1\times10^{-7}) + (78{,}900\times1\times10^{-7})$.

As k_{obs} at pH 7 and 25°C was determined as 0.0228 d^{-1}, k_0 = 0.003 d^{-1}.

The values of k_0, k_{H30+} and k_{OH-} allow the first order rate constant for hydrolysis (k_{obs}) to be estimated at any pH.

The experiment at pH 7 was carried out at three temperatures. Analysing these data using the Arrhenius equation allows value of k_{obs} at any given temperature to be extrapolated[2]. A plot (not shown) of ln k_{obs} versus 1/T (in K) revealed that the activation energy for the reaction was around 83,500 J/mole. The value of k_{obs} at pH 7 can then be estimated to be around 0.00526 d^{-1} at 12°C (equivalent to a half-life of around 132 days) and 0.00361 d^{-1} at 9°C (equivalent to a half-life of around 192 days).

The variation of the k_{obs} at pHs other than 7 is more difficult to estimate as it is not known if the same activation energy would apply to other pHs and this will vary with pH. However, as a first approximation the variation of the k_{obs} at other pHs can be assumed to be similar[3] to that seen at pH 7 (i.e. the value of k_{obs} at 12°C would be expected to be smaller than the value at 25°C by a factor of 0.0228/0.00526 = 4.3 and the value of k_{obs} at 9ºC would be smaller than the value at 25°C by a factor of 0.0228/0.00361 = 6.3).

Based on the above assumptions, plots of the variation of the expected hydrolysis half-life with pH can be constructed at temperatures of 9, 12 and 25°C. This is shown in Figure 1. As can be seen from the plot the hydrolysis half-life is predicted to reach a maximum just over 30 days at 25°C, around 130 days at 12°C and around 190 days at 9°C. It can also be seen from Figure 1 that the hydrolysis half-life is predicted to be above 40 days at pHs between approximately 6.3 and 7.9 at 12°C and pHs between approximately 6.1 and 8.1 at 9°C. The hydrolysis half-life is predicted to be above 60 days at pHs between approximately 6.5 and 7.7 at 12°C and pHs between approximately 6.3 and 7.9 at 9°C.

[2] The Arrhenius equation states that $k_{obs}=Aexp(-Ea/RT)$, where A is the pre-exponential factor, Ea is the activation energy of the reaction, R is the universal gas constant and T is the absolute temperature. Thus a plot of ln k_{obs} versus 1/T allows the values of Ea (-slope) and A (intercept is ln A) to be estimated and the value of k_{obs} to be calculated at any given temperature.

[3] Arrhenius plots indicate that at pH 5 the activation energy would be around 56,100 J/mole and at pH 9 would be around 93,600 J/mole. The average of these two values is 74,900 which is similar to that estimated at pH 7. The registration dossier gives slightly lower activation energies for pH 5 and 9 (59.4 kJ/mol and 36.1 kJ/mol) – the reason for this discrepancy is not clear at present.

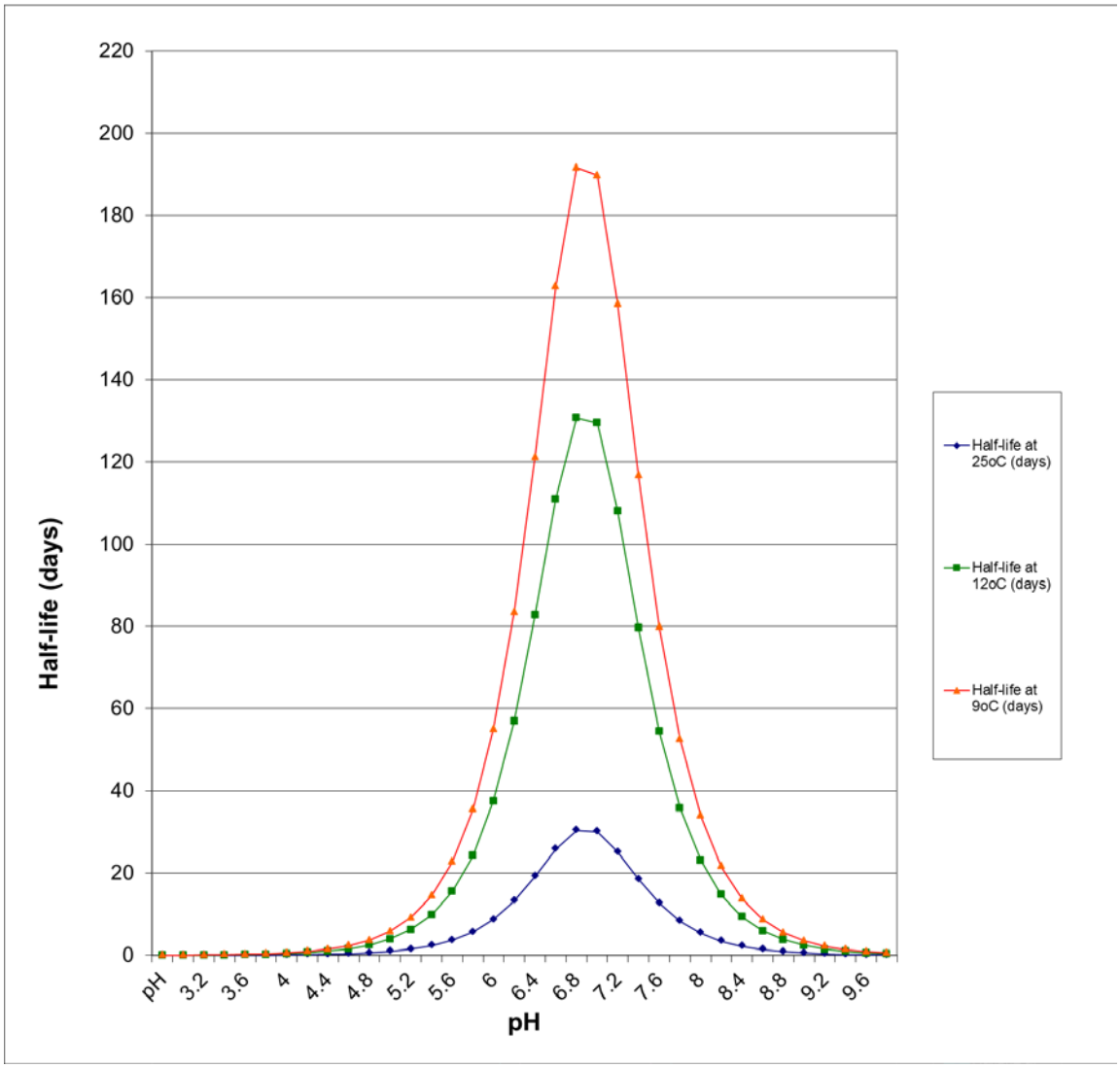


Figure 1: Variation of hydrolysis half-life with pH and temperature for L4

The Registrant(s) have performed a similar calculation (pers. comm, Jan 2016). They calculate that the pH range where the half-life exceeds 40 days is between 6.37 and 8.09 at 12°C, with a maximum half-life of 148 days occurring at pH 7.23. The 60 day threshold is exceeded between pH 6.56 and 7.91. At 9°C, the 40 day threshold is exceeded between pH 6.25 and 8.28, with the 60 day threshold exceeded between pH 6.43 and 8.10 (maximum half of 209 days at pH 7.27). At 25°C there are no values where the 40 (or 60) day thresholds are exceeded. The Registrant(s) highlight that the error in the calculations is greatest at the lower temperatures (9 and 12°C) because of the temperatures used in the experiment itself.

These calculations used the E_a values noted in the footnote on the previous page, which are slightly different to the values used by the eMSCA. The pH range where the respective thresholds are exceeded shift slightly (by around 0.3 pH units) but the width of the pH range for the exceedance remains the same (e.g. around 1.6 pH units for 12 degrees and 40 days).The eMSCA notes that for some other siloxanes, for example D4 and D5, the rate of hydrolysis is known to be significantly impacted by DOC.

Read-across to hydrolysis of Octamethyltrisiloxane (L3)

A study on the hydrolysis of octamethyltrisiloxane (CAS No 107-51-7) has been included as a read-across to decamethyltetrasiloxane. The study is given a reliability score of 1. Radiolabelled substance was used. Experiments were carried out at pH 5, 7 and 9, and at different temperatures.

Recoveries in the experiments at pH 5 and 9 were high, ranging from 88 to 95% with an overall average of 91%. In the pH 7 experiments, recoveries were lower and more variable, in the range 62 to 75%. This was attributed to partitioning of the substance into the headspace of the tubes used, which was more significant over the longer duration of experiments at this pH. For these experiments, the losses by volatilisation were modelled by non-linear regression using a two-box model, and the calculation of the rate constants and half-lives adapted accordingly (the pH 5 and 9 rate constants were calculated using linear regression).

The half-lives obtained from the study are presented in Table 11.

Table 11: Hydrolysis half-lives of L3

pH	Temperature	Half-life (hours)	Equivalent first order rate constant k_{obs} (day^{-1})
5	10	15.3	1.09
	25	5.09	3.27
	35	2.42	6.99
7	10	1,468 (61 days)	0.0113
	25	329 (13.7 days)	0.0506
	35	140 (5.8 days)	0.119
9	10	68.6 (2.9 days)	0.24
	25	9.76	1.70
	35	2.85	5.84

The initial products of hydrolysis are also unstable in water. The ultimate products of hydrolysis were dimethylsilanediol (detected) and trimethylsilanol (inferred, not detected due to the position of the radiolabel in the parent substance).

The half-life for hydrolysis depends on the temperature and the pH. A hydrolysis half-life of 13.7 days (pH 7 and 25 °C half-life at pH 7) and 61 days (pH 7 and 10°C) was measured. Since a temperature of 12 °C is relevant for the freshwater environment, the hydrolysis half-life has been calculated at pH 7, equating to 52 days at 12 °C.

The experimental hydrolysis half-life of L3 is slow, exceeding the REACH Annex XIII criteria for persistence (P), and the test results can be used in a weight of evidence approach underpinning the slow hydrolysis of L4.

In summary, experimental hydrolysis half-lives were determined for L4 with OECD TG 111, showing hydrolysis half-life of 30 days at pH 7 and 25 °C. Registrant(s) conclude that the L4 is not persistent in the aquatic environment. However, at pH 7 and 10°C a long half-life of around 165 days has been demonstrated. Since a temperature of 12°C is relevant for the freshwater environment, the hydrolysis half-life has been calculated at pH 7, equating to 130 days at 12°C. -

Furthermore, experimental hydrolysis half-life for L3 of 61 days (pH 7 and 10°C) and calculated half-life of 52 days (pH 7 and 12°C) can be used in a weight of evidence approach underpinning the slow hydrolysis half-life of L4.

The hydrolysis rates for the cyclic siloxanes D4 and D5 were also assumed to be impeded by dissolved organic carbon (DOC) (ECHA, 2015). DOC is present in the environment. Therefore, the hydrolytic half-lives for L4 may be longer than suggested by the results in pure water.

No information is available on the potential for hydrolysis of L4 in sediments. It is expected that adsorption onto the sediment will reduce the potential for hydrolysis in the sediments compared to water, as is the case for some cyclic siloxanes e.g. D4 and D5 (ECHA, 2018).

7.7.1.1.2. Phototransformation / photolysis

7.7.1.1.2.1. Phototransformation in air

There are no measured data on phototransformation in air for L4 in the registration dossier. The registration dossier includes the results of calculations of the rate constant for the reaction of L4 with hydroxyl radicals in air using the AOPWIN (v1.92) program. The calculated rate constant is 1.5×10^{-12} cm^3/molec sec. For a 24-hour average concentration of OH radicals of 5×10^5 molec/cm^3, this corresponds to a half-life of 11 days. The Registrant(s) note that there is some uncertainty associated with the result, as the calculation method has not been validated for this type of substance (siloxane).

7.7.1.1.2.2. Phototransformation in water

No information on phototransformation in water

7.7.1.1.2.3. Phototransformation in soil

No information on phototransformation in soil

7.7.1.2. Biotic degradation

7.7.1.2.1. Biodegradation in water

7.7.1.2.1.1. Estimated data

No estimations on the biodegradation of L4 in water have been carried out as adequate experimental data are available.

7.7.1.2.1.2. Screening tests

No screening tests on the biodegradation of L4 in water are available. Screening test results for L3 are read across to L4.

An OECD Test Guideline 310 ready biodegradability test is reported in the registration dossier for L3 (registration dossier, 2009). The test was performed in accordance with GLP. Activated sludge was collected from a wastewater treatment facility treating mainly residential wastewater. Following preconditioning, the activated sludge was diluted in test medium to give a total suspended solids concentration of 4 mg/l. The initial concentration of the test substance was 20 mg/l.

The tests were carried out in glass serum bottles with a nominal volume of 160 ml. After addition of the test substance the bottles were sealed with butyl rubber septa and crimp caps. Biodegradation was measured by carbon dioxide evolution. Positive control experiments were conducted using sodium benzoate.

No biodegradation was observed (as CO_2 evolution) for the test substance over the 28-day test. The reference substance was biodegraded by 96.5% over the 28 days. The test fulfils the validity criteria, and the study is given a reliability score of 1.

Overall, the read-across suggests that L4 is not readily biodegradable in a standard screening test system.

<u>Other considerations on biodegradation screening tests</u>

The Registrant(s) have included on ECHAs disseminated page in the summary of ready biodegradation a table of results on substances that fall within the Reconsile Siloxane Category of substances. The linear siloxanes L2, L3, L4 and L5 fall within this category along with many other siloxanes. Within this group, there is in general no evidence of significant biodegradation for any of the members. The results reported in the table have not been further assessed by the eMSCA.

7.7.1.2.1.3. Simulation tests (water and sediment)

Water

No data on simulation tests in water are included in the registration dossier.

Sediment

Data on simulation tests in sediment are not available for L4 but for L2, L3, D4 and D5.

Read-across to sediment simulation study on L3 (OECD 308)

In the substance evaluation decision for L4, a sediment simulation test (OECD 308) at 12°C was requested. Aerobic and anaerobic transformation in aquatic sediment systems, including the identification of transformation products, was to be performed. Test results from an OECD TG 308 sediment simulation study with L3 have been made available to eMSCA in February 2021. The eMSCA notes that there are some issues with the test, which are discussed further below.

A comparison of the properties of L4 with those of L3 reveals that L4 has a vapour pressure below that of L3, but a higher Henry's law constant at 12°C. Therefore, a higher volatility for L4 than L3 from water can be expected. Both substances have a similar predicted long residence time in air once volatilised. The potential for adsorption of L4 (as measured by the log Koc) is however higher than that of L3, which may counteract to some extent the higher volatility of L4 compared to L3 when the whole sediment is considered. The hydrolysis half-life in water is also longer for L4 than for L3.

Table 12: Comparison of properties of L4 with L3

Property	Value	
	L4	L3
Molecular formula	$C_{10}H_{30}O_3Si_4$	$C_8H_{24}O_2Si_3$
Molecular weight (g/mole)	310.69	236.53
Water solubility at 23°C (mg/l)	0.0067	0.034
Vapour pressure at 25°C (Pa)	73	530
Henry's law constant at 12°C (Pa m3 mol^{-1})	$2.59x10^6$	$1.62x10^6$
log Kow at 25°C	8.21	6.6
log Koc	5.16	4.34
Half-life in air (days)	11	13
Hydrolysis half-life at pH ~7 (days)	165 at 10°C 130 at 12°C 30 at 25°C	61 at 10°C 52 at 12°C 13.7d at 25°C
Ready biodegradability	No	No
Half-life in sediment (days)	Expected to be >>180 days by read-across	6.91 years

Study setup

The study on aerobic transformation in aquatic sediment systems was performed according to OECD TG 308 to GLP standard (DOW, 2020) at 12°C for 140 days. The Registrant(s) assess the study to be Klimisch score 1 (valid without restrictions). This used ^{14}C-radiolabelled L3 with a chemical purity of 99.9%, a radio-chemical purity of 99.4%, specific activity 64.5 mCi/mmol. Two sediments were used: Calwich Abbey Lake, UK (silt loam) and Emperor Lake, UK (sandy clay loam). When compared to the quality criteria of OECD TG 308, point 13, it is stated that 'recoveries should range from 90% to 110% for labelled chemicals and from 70% to 110% for non-labelled chemicals. Most samples in the study are within the mentioned range. The samples with recoveries outside the quality criteria were the day 7 samples from the Calwich Abbey Lake sediments, with a recovery of 81.6%,

and the samples from Emperor Lake from day 57 and to the completion of the study (140 days), with a recovery from 85.5% - 89.1%. In our assessment, we conclude that the study does not completely fulfil the quality criteria for all samples used. Although some of these values fall outside the 90% to 110% range of recovery targeted for radiolabelled chemicals, the recoveries obtained seem reasonable when allowing for the challenging properties of L3, including low aqueous solubility and high air-water partition coefficient. Also, the deviation from the targeted range is small and the study is considered by the eMSCA as reliable despite these issues.
The characteristics of the two sediments are detailed in Table 13.

Table 13: Characteristics of the two sediments used in the OECD TG 308 study with L3

Property	Calwich Abbey Lake Sediment	Emperor Lake Sediment
% Organic Carbon	4.7% w/w	2.0% w/w
pH (water/0.01M $CaCl_2$)[4]	7.0 / 6.9	6.5 / 5.6
Textural Class	Silt Loam	Sandy Clay Loam
Particle Size Distribution: Sand	27.1% w/w	63.7% w/w
Particle Size Distribution: Silt	70.4% w/w	16.1% w/w
Particle Size Distribution: Clay	2.5% w/w	20.2% w/w

Test system flasks were prepared as follows: to 250 mL Erlenmeyer-type flasks, approximately 50 g dry weight (d.w.) Calwich Abbey Lake sediment or 60 g d.w. Emperor Lake sediment[5] was added. The sediments were topped with the corresponding surface water to the 225 mL mark. This gave a sediment layer thickness of around 2 cm. The test systems were then equilibrated for 2 to 3 weeks at 12 °C.

Aeration of test system

The oxygen saturation in the control vessels for Calwich Abbey Lake and Emperor Lake was measured before and after aeration events. While the Calwich Abbey Lake sediments had an average oxygen saturation (%O_2) of 4.8% and 53%[6] in the controls at the start and end of each aeration event respectively, the Emperor lake sediment controls had an average % O_2 of 19 % and 55%. The aeration events were performed more frequently for the Calwich Abbey lake sediments than for the Emperor lake sediments due to the lower oxygen consumption in the Emperor lake system and had an average interval 2,2 days vs 3,5 days. Both of the values after aeration are lower than desired for the formation of an aerobic layer in the surface of the sediment.

The lower levels were suggested by the Registrant(s) to be a result of biodegradation of the diethylene glycol methyl ether (DEGME) solvent. By comparison, the typical oxygen content in the aerobic layer is described in the OECD guideline as ranging from 7 – 10 mg/L, approximately equivalent to 65- 93% saturation at 12 °C. During the exposure period, the dissolved oxygen (DO) probe was moved further away from the water: headspace interface by switching to a longer needle, as it was realized that the initial DO-probe placement was not yielding representative measurements. At the start of the study, the pH of the overlying water was 7.0/6.9 (water/0.01M $CaCl_2$) for the Calwich Abbey Lake and 6.5/5.6 (water/0.01M CaC_{l2}) for Emperor Lake. At exposure termination, pH increased to average values of 7.5/7.38 and 7.35/6.95 (water/0.01M $CaCl_2$), respectively.

Application of test material

[4] pH at Day0, Pre-acclimation pH not available.
[5] Sediment wet weights are quoted as 143 – 151 g Calwich Abbey , and 118 – 122 g Emperor Lake
[6] The measurements up to day 25 showed an increase from 9.2 to 37% for the aeration events, but the 4.8% and 53% is considered more reliable due to a better placed probe.

Following the acclimation period, natural water corresponding to the origin of the sediments was added at 12 °C to fill each test vessel. From each test vessel 20 mL of water was then removed to give a consistent headspace. Prior to dosing approximately 60 mL of water was removed, and the associated sediments spiked with 10 µL of L3 in DEGME[7] (applied loading approximately 0.005% *v*/*v*). Spiking was performed in 1 µL aliquots using a microsyringe at multiple positions on the surface of the sediment (using an approximate grid pattern of 3-4-3). Spiking provided an initial nominal concentration of 150 ppb (ng ^{14}C L2 per g of sediment/ dw). Following a query from the eMSCA, the Registrant(s) explained that the application rate was selected based on the available amount of test substance and the required analytical sensitivity resulting from the specific activity of the radio-labelled test substance.

There were 17 flasks dosed with L3 for each sediment (allowing for eight planned sampling intervals in duplicate and one spare vessel). Four control flasks were prepared with 10 µL of DEGME. Immediately following spiking, the reserved water was replaced in the vessels leaving a 20 mL head space void. Vessels were then closed tightly with a septum cap and incubated in the dark at 12 °C for 140 days, except when removed from the incubator during regular aeration events.

The ^{14}C-radiolabelled L3 application solution was supplied to the test laboratory as a solution in DEGME and was used directly without any dilution in the study. The solution was characterized (non-GLP) by the supplier prior to shipment. Concentration, specific activity, and radiochemical purity were reported on the provided certificate of analysis (CoA).

Sampling and collection of volatiles and evolved ^{14}CO2

Sampling was performed at day 1, 7, 28, 57, 77, 98, 119 and 140 for both Calwich Abbey Lake (CAL) and Emperor Lake (EL). Chemical analysis was performed using liquid scintillation counting (LSC) for ^{14}C, and HPLC-RAM for speciation. Oxygen and pH were only measured in the control vessels, with values assumed to be representative of the exposure vessels containing L3.

At each sampling interval, volatile compounds were captured in sequential traps that comprised 1) dry ice/acetone bath, 2) two vials containing *Perkin Elmer Ultima Flo M cocktail* and, finally, 3) a carbon dioxide trap containing the product *Oxosol C14* cocktail from National Diagnostics for trapping $^{14}CO_2$. Traps were rinsed with tetrahydrofuran (THF) solvent in order to recover any residual radioactivity.

Table 14,Table 15 and Table 16 summarize the results of the study. Abrupt initial losses from the systems were observed, with 14 % of ^{14}C activity lost from the Calwich Abbey Lake system from day 0-7 and 10% during the rest of the study (days 7-140), while 9,3% was lost from the Emperor Lake system from day 0-7 and a further 3.8% during the rest of the study (days 7-140). The early losses were considered to be a consequence of the volatile nature of the test substance. The radioactivity associated with the sediment, water and air compartment is presented in Table 14. All values were calculated relative to the total amount of applied radioactivity as ^{14}C-L3, which was based on LSC analysis of the dosing solution, determined as 1.42x10^7 dpm (equivalent to 6.4 µCi as ^{14}C-L3).

Results

[7] Diethylene glycol methyl ether (DEGME), is indicated in the report to be readily biodegradable and non-toxic to micro-organisms. The report indicates that as it is water miscible and has a specific gravity greater than one, this facilitated the distribution of L3 to sediment (and thereby mitigated loss through volatilization).

Table 14: Distribution of ^{14}C in the two sediments at the end of the study

Media	Calwich Abbey Lake Sediment (day 140)	Emperor Lake Sediment (day 140)
% Air – CO_2 + aeration loss	2.2	2.5
% Water	4.0	5.2
% Sediment	95.5	81.4
% Recovery	101.7	89.1

Chromatographic profiling samples from overlying waters were mainly generated using a solid phase extraction (SPE) method. However, for the vessels sacrificed at Day 57 of incubation only direct HPLC analysis was conducted. Interpretation of the chromatograms was made difficult by the low levels of ^{14}C activity in the overlying waters (mostly under ~3,000 dpm/g for the (CAL) system and only slightly higher in the (EL) system) and significant variations in the retention times for some of the peaks. Further, in several cases the combined 14C activity for the chromatographic peaks was below 80% of the amount injected, especially for the CAL waters.

Therefore, from Day 77 and continuing through the remaining sampling intervals, 50 mL volumes of overlying water were extracted by SPE and eluted with THF in order to increase sensitivity for the water analysis. In these sample extracts (4 time points x 2 vessels from each sediment system) the injected 14C activity ranged from approximately 5,000 dpm to 10,000 dpm, and the average ratio of recovered to injected radioactivity was 91.5% for EL samples, and 95.4% for CAL samples.

Speciation analysis of SPE cartridge extract from the overlying water, solvent extraction of sediments and cryogenic trapping were performed by HPLC with flow scintillation detection. Observed peaks in combination with known radioactive content of each extract were used to calculate the percentage of applied radioactivity (normalised as above) that corresponded to parent L3, trimethyl silanol (TMS), Dimethylsilanediol (DMSD) and pentamethyldisiloxanol (PMDS).

Speciation data are presented in Table 15 as fractions of applied radioactivity. Both results from direct injection and SPE are available for overlying water and sediments in the study report, but only results from SPE extraction are included in Table 15 since the SPE was considered necessary for reliable sample preparation in overlying water.

TMS was the major transformation product (resulting from hydrolysis and identified[8] via mass spectrometric analysis). TMS, DMSD and PMDS increased in overlying water throughout the experiment and were present at up to 3.1, 1.3 and 0.5% in the overlying water at the end of the experiment. L3 was found at up to 0.42% at day 140 in overlying water and was the only one of the species found in sediments. In both sediment systems, the applied radioactivity was overwhelmingly present as L3 in sediment. All percentages in this paragraph are normalised to the applied radioactivity.

The $^{14}CO2$ levels are found mostly in overlying waters at early stages of the study but more is eventually found in the headspace of the vessels. The amount of applied radioactivity present as CO_2 was 0.12% and 0.14% in Calwich Abbey lake sediments and Emperor lake sediments respectively. The limited amounts of carbon dioxide observed in the study were considered to be consistent with the results from a screening test (OECD TG 310) where no biodegradation was observed.

[8] No indication was given in the report that a certified analytical reference standards was using to verify this identification

Table 15: Chemical speciation in the two sediments at the end of the study (day 140 - averaged) as fractions of applied radioactivity

Media	Species	Calwich Abbey Lake Sediment	Emperor Lake Sediment
Overlying water	% L3	0.3	0.4
	% TMS	2.1	2.9
	% PMDS	0.5	0.5
	% DMSD	1.1	1.3
Sediment	% L3	89.7	75.5
	% TMS	0	0
	% PMDS	0	0
	% DMSD	0	0
Total	% L3	89.9	75.7
	% TMS	2.1	2.9
	% PMDS	0.5	0.5
	% DMSD	1.1	1.3

Data generated were normalised using the total applied radioactivity residue to the test systems at day 0. It should be noted that the values at day 0 also show the losses occurring through vessel dosing and volatile loss as the system re-equilibrated. As Table 16 shows, some loss of test substance did occur, and the applied radioactivity is mostly found as L3 in sediment during the study period. The values for applied radioactivity in sediment ranged from 77.2% to 106.6% for Calwich Abbey Lake sediment, and from 78.2% to 90.6% (averages of duplicate vessels) for Emperor Lake sediment.

The significantly wider range in the Calwich sediment was associated with a few values of 100% or greater for individual vessels, and exceptionally large deviations between duplicate vessels (15% to 26%) for samples from day 57, 77, and 98. Aside from the possibility that these few vessels received more spiking solution than the rest, which seemed unlikely since the phenomenon was not observed for any Emperor vessels, the authors considered that the most likely explanation was sampling error. However, it was also possible that the total 14C activity in the original sediment was not uniformly distributed in the test vessel prior to sub-sampling. As these deviations were not observed among the Emperor Lake vessel duplicates, the variation might be associated with the differing texture (more sandy) and lower OC content of this sediment. Unfortunately, the sampling design does not allow further testing of this hypothesis.

Table 16: Percentage of applied radioactivity associated with the sediment compartment of each test system over the exposure period of the OECD 308 study. Averages of duplicate vessels sacrificed on each sampling day

Sample day	Calwich Abbey Lake		Emperor Lake	
	Sediment	Recovery %	Sediment	Recovery %
1	85.7	90	90.6	98.2
7	77.2	81.6	86.8	92

28	97.8	100.5	86.5	91.6
57	98.3	102	81.1	87.8
77	106.6	111	78.2	85.5
98	97.3	91.9	78.3	86.5
119	87.8	93.2	78.6	87.3
140	95.5	101.7	81.4	89.1

% recovery calculated relative to total applied radioactivity

Non-extractable residue (NER)

NER in the CAL and EL sediments was determined by applying 0.1M HCl to a portion of the sediment, following extraction with tetrahydrofuran (THF). The HCl extract was analysed by LSC to determine the total 14C activity remaining after THF extraction. In the CAL sediment, the HCl extractable fraction ranged from 6.3% to 10.9% (maximum 9.8% excluding vessel CAL-19) for all vessels. Sediments from vessels sacrificed at incubation Day 57 showed values below 8.0% mostly, with values increasing for some vessels sacrificed on Day 77 or later.

For the EL sediments, the HCl extractable fraction was slightly lower, ranging from 5.4% to 8.5% across all vessels and showing no distinct trend with time. Overall, these low values and general lack of temporal trends, along with a modest degree of transformation of parent L3, suggests that most of this residual activity was likely associated with the residual THF entrained in the sediment. Thus, the apparent formation of NER was low or non-existent on the time scale of this study.

Kinetics

The Registrant(s) provided degradation pseudo first order half-lives from the study. calculated according to the FOCUS guidance (2014) that states:
"Loss of mass balance due to not accounting for volatiles or bound residues would not affect the kinetic evaluation procedure as long as the sink data (sum of observed data for identified metabolites not specifically included in the fit as compartments, unidentified minor metabolites, organic volatiles, CO2 and bound residues) is not included in the fit. However, losses specific to a particular substance, whether partly or completely unaccounted for, may not only impact the kinetic evaluation of the substance itself, but also any degradation products further down the metabolic pathway, as the route scheme would be affected."

The kinetics calculations were performed using the Hockey-stick model (FOCUS, 2014) and demonstrate that the degradation of L3 followed a bi-phasic model. The hockey stick model with single first order kinetics in each phase was then used to calculate the half-lives. This calculation used all the samples and also took account of volatilisation that occurred at the start of the test, and the degradation follows first-order kinetics independently before and after a break point. The measured total radioactivity per sediment mass at each sampling time was normalized by the total applied radioactivity (i.e., 1.42×10^{7} DPM as 14C-L3) per mean sediment mass (116.4 and 140.1 g for Emperor Lake and Calwich Abbey Lake, respectively); thus, the radioactivity applied per sediment mass was 1.22×10^{5} and 1.01×10^{5} DPM/g-ww, respectively.

The first order kinetic model was not applied to normalized L3 concentrations in Emperor Lake sediment because the model was not able to reproduce the initial drop in normalized non-specific total radioactivity values (NTR), as shown in Figure 2. For Calwich Abbey, the profile of normalized L3 does not show a trend that is suited for mono-phasic or bi-phasic approach (Figure 3). The calculations for Emperor Lake was optimized with measured concentrations of L3 and normalized concentrations of degradation products. For Calwich Abbey lake, however, it was considered not reasonable to use either total radioactivity or

L3 concentration, so only the normalized concentrations of degradation products were used.

Due to the variability of total radioactivity in the wet sediments from individual test vessels following the removal of the overlying water, kV and k1 could not be reliably calculated from measured L3 or total radioactivity. The main issue was the variability associated with the determination of total radioactivity in the wet sediments from individual test vessels following the removal of the overlying water. Instead, normalized concentrations of degradation products were used for the purpose of kinetic parameter estimation, as the method was shown to also yield consistent outcomes for the Emperor Lake system.

Figure 2: Log-linear regressions of normalized concentration of L3 in the Emperor Lake sediment system during the incubation period: (a) monophasic and (b) biphasic approaches.

Figure 3: Log-linear regressions of normalized concentration of L3 in the Calwich Abbey Lake sediment system during the incubation period: (a) monophasic and (b) biphasic approaches.

Table 17: Degradation half-lives for L3 in the two sediments used in the OECD 308 study calculated using the FOCUS guidance

	Calwich Abbey Lake Sediment	Emperor Lake Sediment
Degradation half-life (days) Optimized with measured concentrations of L3	-	1180 3.22 yrs
Degradation half-life (days) Optimized with normalized concentrations of degradation products	2532 6.91yrs	1398 3.83 yrs
Average	**6.91 yrs**	**3.5 yrs**

A substantial proportion of the substance was present outside of the sediment-water system. L3 retained in the sediment degraded slowly and very little was present in water. TMS, PMDS and DMSD were detected in water and TMS was the dominant species in this compartment. On ECHA's dissemination page Registrant(s) state that the intermediate siloxane hydrolysis/degradation products and silanol hydrolysis/degradation product may also meet the screening criteria for persistence (P/vP) in the sediment compartment.

Different half-lives are observed in the two sediments tested. A part of the explanation for this may be the difference in organic carbon content, since hydrolysis might be attenuated by adsorption to dissolved organic matter and particulates. The hydrolysis rates for the cyclic siloxanes D4 and D5 are also assumed to be impeded by DOC (MSC opinion for D4 and D5– (ECHA 2015). The Calwich Abbey lake sediments have a higher amount of carbon and also the slowest degradation.

Further, the two sediments also have some differences in their pH values. The Calwich Abbey Lake sediment had a pH of 7.04 and 6.89 (water and CaCl2, respectively) at the start of the test and ended at 7.38 and 7.08 at Day 141. The Emperor lake sediment had a pH of 6.51 and 5.56 (water and $CaCl_2$, respectively) at the start of the test and ended at 6.95 and 6.03. In the hydrolysis test on L3, pH was shown to have a dramatic effect on the hydrolytic half-life; so that a deviation above or below pH 7 will lead to increased hydrolysis. The Calwich Abbey lake sediment thus has an initial pH where L3 would likely be more hydrolytically stable.

Generally, the longer half-life is preferred for comparison to the persistence criteria in REACH Annex XIII. In this case both sediments are considered to be representative. Therefore, the eMSCA concludes that the half-life from the Calwich Abbey Lake sediment system of 6.9 years should be used to represent the half-life for L3 in sediment. This is also the same value as the Registrant(s) use in their exposure assessment.

Despite the problems encountered during the test and deviations from validity criteria, the study is considered reliable, and the degradation half-life demonstrate that L3 is very persistent

Data from further simulation studies

Information on the degradation in sediment is available on ECHAs dissemination page for three related substances, the linear siloxane hexamethyldisiloxane or L2 (CAS No 107-46-0) and the two cyclic substances octamethylcyclotetrasiloxane or D4 (CAS No 556-67-2) and decamethylcyclopentasiloxane or D5 (CAS No 541-02-6). PBT assessments have been produced previously for both D4 and D5 which included a detailed evaluation of the persistence, and both substances have been identified as SVHC due to PBT and vPvB

properties (MSC SVHC supporting document for D4 and D5 (ECHA 2018). The data available for L2, D4 and D5 are summarised in Table 18, along with the data for L4.

Table 18:Comparison of properties of L2, D4 and D5 with L4

Property		Value		
	L4	L2	D4	D5
Molecular formula	$C_{10}H_{30}O_3Si_4$	$C_6H_{18}OSi_2$	$C_8H_{24}O_4Si_4$	$C_{10}H_{30}O_5Si_5$
Molecular weight (g/mole)	310.69	162.38	296.62	370.8
Water solubility at 23°C (mg/l)	0.0067	0.93 mg/L	0.056	0.017
Vapour pressure at 25°C (Pa)	73	5500	132	33.2
Henry's law constant at 25°C	6.39×10^6	$0.78x10^6$	1.21×10^6	3.34×10^6
Henry's law constant at 12°C (Pa m3 mol^{-1})	$2.59x10^6$	$0.37x10^6$	n.a.	n.a.
log Kow at 25°C	8.21	5.06	6.49	8.03
log Koc	5.16	3.00	4.22	5.17
Half-life in air (days)	11	11,5	12.7-15.8	10.4
Hydrolysis half-life at pH ~7 (days)	165 at 10°C 130 at 12°C	17.4 at 10°C 4.8 at 25°C	16.7 at 12°C	315 at 12°C
Ready biodegradability	No	No	No	No
Half-life in sediment (days)	Expected to be >>180 days by read-across	192 days (first order kinetics) and 360 days (HS - FOCUS kinetics) at 12 °C (whole system).	~242 days at 24°C (aerobic conditions) ~356 days at 24°C (anaerobic conditions)	~1,200-2,700 days at 24°C (aerobic conditions) ~800-3,100 days at 24°C (anaerobic conditions)

Read-across to sediment simulation study (OECD 308) on L2

Test results from an OECD TG 308 sediment simulation study with L2 are available and have been used as supporting study by the Registrant(s) in their dossier. The eMSCA notes that there are some issues with the L2 test, especially regarding recovery and mass balance.

L4 has a vapour pressure below that of L2 but a Henry's law constant higher than that for L2, indicating a higher volatility for L4 than L2. The potential for adsorption of L4 (as measured by the log Koc) is however higher than L2, which may to some extent counteract the higher volatility of L4 compared to L2 when the whole sediment is considered. Both substances have a predicted long residence time in air once volatilised. The hydrolysis half-life in water is longer for L4 than for L2, with 165 and 17.4 days at 10°C respectively. As L2 has been demonstrated to have a long half-life in sediment it can reasonably be assumed that the same will apply to L4 and that the half-life will be similarly >180 days.

For L2, an aerobic transformation in aquatic sediment systems study was performed according to OECD TG 308 to GLP standard (DOW, 2019). The Registrant(s) assess the study to be valid without restrictions (Klimisch score 1). ^{14}C-radiolabelled L2 with a radio-chemical purity of 96.9%, specific activity 75.4 mCi/mmol and concentration of 0.5 mCi/mL

was used in the study. Two sediments were used: Calwich Abbey Lake, UK (silt loam) and Emperor Lake, UK (sandy clay loam). However, in our assessment we conclude that the study does not fulfil the validity criteria of OECD TG 308 where (point 13) it is stated that 'recoveries should range from 90% to 110% for labelled chemicals and from 70% to 110% for non-labelled chemicals.'

Sampling of duplicate test vessels, sacrificed at each sampling time point, was performed at day 1, 7, 18, 44, 74 and 99 (Calwich Abbey Lake) and day 1, 7, 20, 41, 70, 100 and 107/108 (Emperor Lake). At each sampling interval, volatile compounds were captured in sequential traps that comprised 1) dry ice/acetone bath, 2) vials containing non specified scintillation cocktails and finally a carbon dioxide trap. A further trap was added early in the study due to the suspected passage of air drawing volatiles (including L2) into the carbon dioxide trap (and consequently causing analytical problems). Traps were rinsed with tetrahydrofuran (THF) solvent in order to recover any residual radioactivity.

Table 19 to Table 22 summarise the results of the study. Significant initial losses from the systems were observed, with nearly 50% of ^{14}C activity lost from the Calwich Abbey Lake system on day 1 and 33% was lost from the Emperor Lake system. These were considered to be a consequence of the volatile nature of the test substance.

During method development with L2 dosed into deionized water, the glass coil cold trap immersed in a dry ice/acetone bath was found to be highly effective at capturing and retaining L2 from a gas stream for a flow rate and time comparable to that used for the regular aeration of the test vessels. The breakthrough of the cold trap was significant for the real test systems, particularly early after dosing, before the L2 had reached equilibrium distribution between the sediment and water.

The Registrant(s) have speculated that the transport mechanism for L2 coming out of the natural waters was different, perhaps involving a particulate phase formed during bubbling that passed through the cold trap and on to the liquid traps. The normalised (to day 1 radioactive recovery) radioactivity associated with the sediment compartment is presented in Table 19.

Table 19:Distribution of ^{14}C in the two sediments used at the end of the study

Media	Calwich Abbey Lake Sediment (day 99)	Emperor Lake Sediment (day 107/108)
% Air	<0.1	<0.1
% Water	22.7	65.7
% Sediment	77.3	34.3
% Recovery (100% = normalisation against day 1 samples)	52.9	68.9

Chromatographic profiling samples from overlying waters and sediments were generated using a solid phase extraction (SPE) method. TMS was the major transformation product (resulting from hydrolysis and identified[9] via mass spectrometric analysis). Two minor peaks were considered to be (a) an impurity of L2 (as this was detected on day 1) and (b) either a degradation product of TMS or of the impurity. The presence of impurities cannot be verified as no purity assessments were performed on the application solution. The limited amounts of carbon dioxide observed in the study were considered to be consistent with the known slow mineralisation of the test substance. As the carbon dioxide levels are

[9] No indication was given in the report that a certified analytical reference standards was using to verify this identification

only depicted graphically (and as DPM[10]), it is unclear what proportion of total ^{14}C this represented.

Table 20:Chemical speciation in the two sediments at the end of the study

Media	Species	Calwich Abbey Lake Sediment (day 99)	Emperor Lake Sediment (day 107/108)
Overlying water	% L2	3.7	0.2
	% TMS	94.6	99.2
	% other	1.7	0.6
Sediment	% L2	73.6	37.6
	% TMS	25.5	61.3
	% other	0.9	1.1
Total	% L2	57.7	13.8
	% TMS	41.2	85.4
	% other	1.1	0.8

Data generated were normalised using the total radioactive residue of the test systems sacrificed on day 1, which were represented as 100% applied radioactivity. Following a query from the eMSCA, the Registrant(s) indicated that the 1 d values are considered to represent the effective dose for the study. Values at 0 d would include the losses occurring through vessel dosing and volatile loss as the system re-equilibrated. As Table 21 shows, significant loss of test substance occurred. There was additional uncertainty in the accuracy of the chromatographic profiling because analyses of radioactive content and radioactive purities, pre- and post- dosing of the application solution, were not reported

Table 21: Percentage of applied radioactivity associated with the sediment compartment of each test system over the exposure period of the OECD TG 308 study

Sample day Calwich A. / Emperor	Calwich Abbey Lake Sediment		Emperor Lake Sediment	
	Total applied radioactivity in sediment	Relative contribution from L2	Total applied radioactivity in sediment	Relative contribution from L2
1	74.3	70.5	67.6	78.7
7	86.1	83.4	67.2	72.4
18 / 20	88.5	85.0	56.0	65.2
44 / 41	84.7	86	57.5	71.9
74 / 70	81.2	77.1	40.7	46.6
99 / 100	77.3	73.6	42.1	41.5
107-8	-	-	34.3	37.6

% recovery calculated relative to day 1 of total AR

10 Disintegrations per minute

Kinetics

The original kinetics calculations in the test report were performed using a first order kinetic model [ln (fraction [L2]t) =-kt] which was applied to the natural log-transformed values of the average and normalised %L2 across all compartments (i.e., whole system data) for the duplicate test vessels at each sampling interval. Values of k were obtained from linear regression, the corresponding first order model is ln (1-fraction [TMS]t)=-kt. The calculated rate constants and half-lives documented in the finalised study report are presented in Table 22.

The Registrant(s) have also supplied supporting information and used the methodology presented in Appendix 11 of FOCUS 2006:2014, where a correction procedure can be applied to account for dissipation by volatilisation. The Registrant's calculations in Table 23 have led to an increase in the half-life of the substance exposed with the Calwich Abbey Lake sediment (from 192 to 360 days) but made little difference to the half-life of the substance tested in the Emperor Lake sediment (increased from 53 to 54 days).

Table 22: Original first-order kinetics calculation for the two sediments in the OECD TG 308 study

	Calwich Abbey Lake Sediment	Emperor Lake Sediment
Total System Rate Constant ($days^{-1}$)	3.61×10^{-3}	1.31×10^{-2}
Total System DT_{50} (days)	192 (90% confidence interval = ± 56 d)	53 (90% confidence interval = ± 17 d)

The revised kinetics demonstrate that the degradation of L2 followed a bi-phasic model. The hockey stick model with single first order kinetics in each phase was then used to calculate the half-lives. This calculation used all the samples and also took account of significant volatilisation that occurred at the start of the test. The Deg50 (whole system) (after adjusting for volatilisation) for the Calwich Abbey Lake sediment was calculated to be 360 days, and 54 days for the Emperor Lake sediment.

Table 23: Degradation half-lives for L2 in the two sediments used in the OECD TG 308 study calculated using the FOCUS guidance

	Calwich Abbey Lake Sediment	Emperor Lake Sediment
Degradation half-life (days)	360	54
Standard error	186	9.0

The eMSCA concludes that there is a significant loss of L2 occurred due to its volatility. This means that a significant proportion of the substance was present outside of the sediment-water system. L2 retained in the sediment degraded slowly. L2 remaining in the water was virtually all hydrolysed, and only TMS was detected to a significant extent in this compartment. The Registrant(s) state that the intermediate siloxane hydrolysis/degradation products, and silanol hydrolysis/degradation product, may also meet the screening criteria for persistence (P/vP) in sediment.

Despite considerable problems with the study data and the analytical problems encountered, the data indicate that the REACH Annex XIII persistence criteria for very persistent (vP) are met for L2.

Comparison with D4 and D5

A comparison of the known properties of L4 with those of D4 and D5 reveals that L4 has a vapour pressure in between D4 and D5. However, the Henry's law constant is higher than that of D4 and D5, so a higher volatility from water can be expected. All three substances have a similar predicted long residence time in air once volatilised.
The potential for adsorption of L4 (as measured by the log K_{oc}) is similar to that of D5, and the hydrolysis half-life for L4 in water is between that of D4 and D5. As both D4 and D5 have been demonstrated to have long half-lives in sediment it can be assumed that the same may apply to L4 and that the half-life will be similarly >180 days. This supports the results of the sediment simulation study performed on L3, demonstrating a long half-life. Still there is some uncertainty based in the structural differences between the substances. It is not known whether the length of linear structure versus the cyclic structure will have the same impact on the degradation in sediment. Substances with linear structures are generally considered more biodegradable than substances with branched and cyclic structure. It is however uncertain if this holds for the siloxanes.

Further support for the expected trend in the linear substances comes from the increasing hydrolysis half-lives for L2, L3 and L4 respectively. Together this indicates that the persistence of siloxanes with increasing chain length will be greater than or at least equal to the shorter chains.

7.7.1.2.2. Biodegradation in soil

A study on the effect of temperature and humidity on the degradation of L4 (decamethyltetrasiloxane) in soil has been carried out (registration dossier, 2014). This study used London soil from Michigan, USA (22% clay, 28% silt, 50% sand, 2.4% organic carbon, pH 7.6). The test substance used was radiolabelled ("mostly on the dimethylsiloxyl moiety") and had a radiochemical purity of 99.21%.

For the experiments, 5 g of air-dried soil was weighed into pre-weighed 25 ml Teflon tubes. The dry soil in the tubes was pre-conditioned for at least one week in containers with controlled humidity atmosphere. The air humidity levels used were 32, 42, 92 and 100% relative humidity (RH). Furthermore, humidity in the atmosphere was the only source of moisture in the study. Each pre-conditioned soil sample was spiked by dropping a solution of the test substance onto multiple positions on the soil surface to give a concentration of 10 µg/g (dry weight basis). The tubes were capped immediately following spiking and thereafter vortexed for five minutes. The tubes were then purged with the appropriate humidity-controlled air for one minute; tubes for the closed system experiments were capped, tubes for the open system experiment were placed into controlled humidity chambers. Experiments were conducted at 22°C, with two additional experiments in closed systems conducted at 4°C and 37°C (at 42% RH).

At the appropriate sampling times, soil was extracted sequentially with tetrahydrofuran and then with 0.1 M HCl/0.01 M $CaCl_2$ aqueous solution. Both extracts were analysed by high performance liquid chromatography coupled to radiometric detection for speciation, and by liquid scintillation counting (LSC) for total radioactivity. Radiolabel not extracted by this method was recovered by combustion of the soil residue using a biological oxidiser, capturing the evolved CO_2 and measuring using LSC.

The average total recovery in the closed system experiments was in the range 89.7 to 114.2%. In the open system (100% RH) more than half of the spiked radioactivity was lost within 3 days, and more than 90% was lost within two weeks.
The half-lives determined for the dissipation of the parent substance at 22°C are shown in Table 24. It can be seen that the rate of degradation was greater as the soil became drier.

Table 24: Degradation half-lives of L4 in soil (closed system)

Relative humidity of air (%)	Half-life (days) at 22°C
100	106.6
92	10
42	4.5
32	3.7

For the two additional experiments, carried out at different temperatures and at a relatively humidity of 42%, the half-lives were determined as 29 days at 4°C, and 1.2 days 37°C. Given the half life of 4.5 days at 22°, these results show a clear temperature dependence in the degradation. In the open system, volatilisation was the predominant process for removal of L4 from soil.

Two degradation products were identified: dimethylsilanediol and trimethylsilanol. The amount of non-extractable residue increased with time and was similar for both soils. The amount increased with increasing temperature, and with decreasing humidity. The Registrant(s) states that the nature of the non-extractable fraction was not completely understood.

The study was not carried out according to GLP and seems to not be compliant with the recommended study design(s) of OECD TG 307 or comply with the stipulations in this guideline for sampling, handling and treatment of soils. Nevertheless, the Registrant(s)s give it a reliability score of 2.

The results of this test show that L4 is degradable in soil but that the rate of degradation is dependent on the moisture content. The test was carried out with dry soil in atmospheres of differing relative humidity. Using a 100% relative humidity atmosphere the half-life approached 107 days at 22°C.

In terms of standardised test conditions (ie. OECD TG 307) recognised in the REACH guidance for persistence determination, it is not possible to benchmark the results of the non-standard soil studies. Therefore, despite being useful supporting information, the standard half-life of L4 in soil remains unknown.

7.7.1.3. Summary on degradation

L4 is predicted to degrade in the atmosphere as a result of reaction with hydroxyl radicals. The half-life for L4 in the atmosphere is approximately 11 days.

The hydrolysis half-life of L4 is dependent on pH and temperature. At pH 7 half-lifes reached a maximum of 30 days at 25°C, 130 days at 12°C and 165 days at 10°C. Experience from other siloxanes (D4 and D5) suggest that DOC may impede the hydrolysis and that the hydrolytic half-life for L4 may therefore be longer than suggested by the results in pure water.

There are no biodegradation screening tests available for L4, but read-across from a structurally similar substance (L3) suggests that L4 will not be readily biodegradable in standard screening test systems.

No information is available on the potential for degradation of L4 in sediments. The simulation study on biodegradation of L3 in sediments (OECD 308) demonstrates a very long half-life for L3 in sediments of 3.5 - 6.91 years at 12°C. The simulation study on L2 (OECD 308) further indicates a half-life in sediment of 360 days for L2, supporting a long half-life for L4 since it is expected to be more persistent than L2. However, the L2 study has several deficiencies and results may therefore be considered not entirely reliable. Based on the reduced hydrolysis and higher organic carbon partitioning, L4 is expected to be more persistent than both L2 and L3 suggesting that L4 will have a half-life in sediments >>180 days. Based on read- across from experimental data for L2 and L3, it can be

concluded that L4 is exceeding the criteria for both persistent (P) and very persistent (vP) of REACH Annex XIII.

Degradation of L4 in soil has been demonstrated in laboratory studies. The half-life in soil seems to increase with increasing water content/humidity. Overall, the available information suggests that the half-life for L4 in soil may, under some circumstances be relatively short (half-life of a few days) but may under others may be expected to be relatively long (107 days). The study is however not easily interpreted and has several issues. L4 is a volatile substance and loss by volatilisation may also occur alongside degradation in water and soil systems.

7.7.2. Environmental distribution

7.7.2.1. Absorption / desorption

The log Koc for L4 has been determined as 5.16 at 23.7°C. This represents the average value measured in three different soils using the OECD Guideline 106 (Adsorption - Desorption Using a Batch Equilibrium Method). The study was carried out according to GLP and was given a reliability score of 1 in the registration dossier.

7.7.2.2. Volatilisation

The substance has a relatively high vapour pressure (73 Pa at 25ºC) and low water solubility (6.7×10^{-3} mg/l at 23ºC). Using these data, the Henry's law constant has been estimated by the eMSCA (using the EUSES program for temperature correction) as 3.29×10^{6} Pa m^3/mole at 25ºC and 1.58×10^{6} Pa m^3/mole at 12ºC, and the dimensionless Henry's law constant (K_{AW}) can be estimated as 1,328 at 25°C and 666 at 12°C.

Values for the Henrys law constant are available in the registration and have been extrapolated to be $5.41x10^{6}$ Pa m^3 mol^{-1} at 20.8°C; $2.59x10^{6}$ Pa m^3 mol at 12°C, based on a Log K_{AW} of 3.22. These values were determined from a study conducted according to a method comparable to an OECD test guideline 117 but not in compliance with GLP. A Henry's law constant of $6,39x10^{6}$ Pa m^3 mol^{-1} at 25°C can also be determined from this Log K_{AW}. The calculation was performed by the eMSCA using a basic temperature correction equation[11] and assumes the same dUAW as estimated for L2. The dUAW is estimated on the basis of two Log K_{AW} determined at different temperatures. This Henry's law constant is considered to be more reliable than the value determined using the EUSES program as it is closer to a Henrys law constant extrapolated at 20°C and follows an expected trend of increasing Henrys law constants with increasing temperature.

The relatively high Henry's law constant indicates that the substance will be volatile in the environment, transferring readily from the water phase to the atmosphere unless already absorbed to organic carbon.

7.7.2.3. Distribution modelling

The distribution in a sewage treatment plant (STP) to different compartment has been estimated using the SimpleTreat model (implemented in EUSES 2.1.2).

[11] logKAW = logKAW25C + deltaUAW*(((1/298.15)-(1/TinK))/(2.303*R))

Table 25: Distribution modelling for STP

Fraction of emission directed to:	%
Air	22.6
Water	4.6
Sludge	72.8
Degraded	0

Air and sludge are the main compartment, with partitioning to water also being significant. Compared to L3, there are higher levels of L4 in sludge and water and lower levels in air.

7.7.2.4. Potential for long-range transport

The potential for long-range transport has been investigated by the eMSCA using the OECD Pov and LRTP screening tool version 2.2[12].

In order to try to assess the effects of the uncertainties, notably the rate of degradation in soil, the modelling was carried out several times using different assumptions for this parameter. The inputs used and the resulting modelled outputs are summarised in Table 26. For all estimates, the molecular weight was set at 310.69 g/mole, the degradation half-life in air at 264 hours (11 days), the half-life in water at 3120 hours (130 days; corresponding to the estimated half-life for hydrolysis in water at pH 7 and 12°C), the log Kow at 8.21 and the log Kaw was set at 2.82 (Kaw = 666). The key outputs for the simulations are displayed graphically in Figure 4.

As can be seen from Figure 4 all of the simulations result in the substance appearing in the upper left-hand quadrant for the characteristic travel distance, which signifies a potential for long range transport. However, the simulations also result in the substance appearing in the lower left-hand quadrant in terms of the transfer efficiency. This means that although the substance has potential for transport over long distances it has a low potential for subsequent deposition in remote areas. The potential for long range transport via adsorption to particulate matter has not been considered in this document.

It is also relevant to note that the substance is predicted to have a relatively long overall persistence for emission to water and this is directly related to the hydrolysis half-life. The rate of degradation assumed in soil has little impact over the predicted long-range transport potential for L4.

Table 26: Summary of long-range transport potential estimated using the OECD Pov and LRTP screening tool

Input assumptions	Modelled outputs		
	Pov (days)[1]	CTD (km)[2]	TE (%)[3]
Half-life in soil = 4,800 hours (200 days)	162 (water)	5,461	0.018
Half-life in soil = 2,880 hours (120 days)	162 (water)	5,460	0.018
Half-life in soil = 1,128 hours (47 days)	162 (water)	5,459	0.018
Half-life in soil = 240 hours (10 days)	162 (water)	5,459	0.018

Notes:

[12] http://www.oecd.org/env/ehs/risk-assessment/oecdpovandlrtpscreeningtool.htm

1) Pov is an estimate of the overall persistence of the substance in the environment. The emission compartment to which the persistence relates is given in brackets.
2) Characteristic travel distance which is an estimate of the distance from a point source at which the chemical's concentration has dropped to 38% of its initial concentration. For all the simulations here the CTD relates to transport by air and so will be dependent on the assumptions made over the half-life in air.
3) Transfer efficiency (TE). This is an estimate of the percentage of emitted chemical that is deposited to surface media after transport away from the region of release

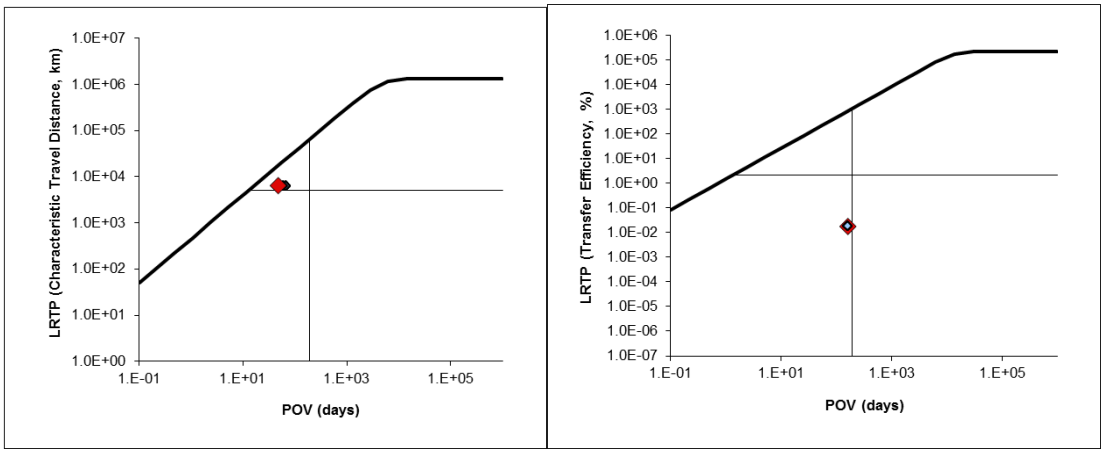


Figure 4: Long-range transport potential of L4

As sorption to particles in air are not likely to be significant for chemicals with a low log K_{OA}[13], this means that associated deposition processes involving particles (wet particle deposition by snow or rain or dry particle deposition) can be ignored in LRTP assessments of L4.
In summary, L4 has a potential for long-range transport via the atmosphere but a low potential for subsequent (re-)deposition in remote areas.

7.7.3. Bioaccumulation

7.7.3.1. Aquatic

7.7.3.1.1. Aqueous study

The registration dossier contains details of a test on the bioaccumulation of L4 in fish, according to OECD test guideline 305 and in compliance with GLP (registration dossier, 2006). Fathead minnows (*Pimephales promelas*) with an average wet weight of 1.29 g at the start of the test, average length 56 mm were used. The test was conducted under flow thro7ugh conditions, in 57 l polyethylene aquaria containing ap7proximately 42 l of test medium using a replacement rate of 10 volume additions per day. The mixing chambers were sealed to limit volatilisation of the substance.

Stock solutions of the ^{14}C labelled substance in dimethylformamide (DMF) were made. Two test concentrations were used. The nominal levels were 0.67 and 6.7 µg/l and the mean measured c7oncentrations were 0.43 and 5.3 µg/l. The duration of the uptake phase of the test was 35 days, with sampling on days 0, 3, 7, 14, 21, 28 and 35. The depuration phase was 28 days, with sampling on days 1, 3, 7, 10, 14, 21 and 28. The concentration of the substance was measured on a whole-fish basis, and in the water samples sampled on the same days. Determination of the concentrations was performed by liquid scintillation counting.

The concentration in fish reached a plateau after 14 days of uptake. The BCF values based on the steady state concentrations in fish and in water were 3,870 l/kg (0.43 µg/l

[13] Log Koa (KOAWIN v1.10 estimate): 5.368

exposure) and 1,610 l/kg (5.3 µg/l exposure). Kinetic parameters were also determined from the test results. In the 0.43 µg/l exposure, the uptake rate (k_1) was 809 l kg^{-1} d^{-1}, and the depuration rate (k_2)7 was 0.211 d^{-1}, giving a kinetic BCF of 3,830 l/kg. In the 5.3 µg/l exposure, k_1 was 218 l kg^{-1} d^{-1}, k_2 was 0.124 d^{-1}, and the kinetic BCF was 1,760 l/kg. The mean lipid content o7f the fish was 3.4% at test initiation and 2.1% at test termination.

The validity criteria for the test were met. The study is given a reliability score of 1.
The study has been evaluated by the eMSCA and is considered valid. However, there are a few issues with the study that warrant further consideration.

- The fish used in the test had lipid contents of 3.4% at the start of the study and 2.1% at the end of the study (the average lipid content would be around 2.8%). The REACH guidance indicates that where possible the BCF values should be normalised to a 5% lipid content. When this is done (using the mean lipid content) the steady state BCF_L would be around 6,910 l/kg (0.43 µg/l exposure) and 2,875 l/kg (5.3 µg/l exposure). Similarly, the kinetic BCF_L would be around 6,840 l/kg (0.43 µg/l exposure) and 3,140 l/kg (5.3 µg/l exposure).

- The concentrations measured in the fish showed a high variability at some of the time points. The difference between the lowest and highest measurement in the replicates at a given time point was up to a factor of 5 or more at some time points during the uptake period and a factor of 50 or more during depuration. This means that there is some uncertainty to a) the steady state concentration in fish and b) the uptake and depuration kinetics. In the registration dossier the values of k_1 and k_2 appear to have been estimated using the simultaneous method (whereby the uptake and depuration curves are fitted together). This may not be the most appropriate way to analyse the data in this case as uncertainties in the concentration during the uptake phase will affect both the k_1 and k_2 values. It may be more appropriate to determine the k_1 and k_2 using the sequential method in this case. In order to investigate the significance of this, the raw data given in the registration dossier have been re-analysed using the sequential method. The concentration data are summarised in Table 27 and are shown graphically in Figure 5 and Figure 6 .

  In the registration dossier the steady-state concentration in fish was determined as the mean concentration measured in the fish on days 14, 21, 28 and 35 for both treatment groups. The mean concentrations (along with standard deviation) over these time periods are summarised below.

<u>0.43 µg/l treatment group</u>

Mean fish concentration: 1,662 ± 784 µg/kg.

The standard deviation to the mean measured water concentration of 0.43 µg/l was ±0.034 µg/l. Thus, the BCF (± standard deviation) that can be estimated from the steady state concentration is as follows.

Mean steady state BCF based (as assumed in registration dossier): 3,870 ± 1,850 l/kg (not lipid normalised). Ignoring the uncertainty in the lipid content, the lipid normalised BCF_L would then be 6,910 ± 3,300 l/kg.

It should be noted that on day 7 of uptake the water concentration was reported to be 4.51 and 4.67 µg/l in two replicates. These values have been omitted from the calculation of the mean exposure concentration (if they are included the mean (± standard deviation) is 1.0 ±1.5 µg/l). The reason for this higher measurement on day 7 is not discussed in the registration dossier but, as can be seen from Table 27, there does not appear to have been a corresponding increase in the concentrations measured in fish around this time point. It is therefore assumed that these values are outliers and have a limited impact on the overall results of the study.

<u>5.3 µg/l treatment group</u>

Mean fish concentration: 8,548 ± 3,310 µg/kg.

The standard deviation to the mean measured water concentration of 5.3 µg/l was ± 0.15 µg/l. Thus, the BCF (± standard deviation) that can be estimated from the above two steady state concentration is as follows.

Mean steady state BCF (as assumed in registration dossier): 1,610 ± 590 l/kg (not lipid normalised). Ignoring the uncertainty in the lipid content (the decline of lipid concentration during the experiment), the lipid normalised BCF_L would then be 2,875 ± 1,050 l/kg.

- The variability in the measured concentrations in fish is also relevant to consider for the kinetic BCF calculation. In the registration dossier, the uptake (k_1) and depuration (k_2) rate constants appear to have been obtained using the simultaneous method (whereby the values of k_1 and k_2 are obtained in one step by simultaneously fitting the entire uptake and depuration curve to the two variables). Although this is an acceptable approach it may not necessarily be the best method for the current data set. The uncertainty in the value of k_2 depends to some extent on the uncertainty in the uptake part of the study as well as the depuration part of the study.

  An alternative way to obtain the values of k_1 and k_2 is to firstly obtain the k_2 directly from the slope of a plot of ln [Concentration in fish] versus time for the depuration phase and then to fit the uptake curve using the value of k_2 obtained as a constant. This has been done for the current data sets and the following concentrations were obtained.

Table 27: Summary of concentrations measured in fish during the BCF study

Day	Concentration in fish (µg/kg)[a]	
	0.43 µg/l treatment group	5.3 µ/l treatment group
Uptake		
0	34,7; 23,0; <LOQ; <LOQ	78,0; 82,9; 72,8; 112
3	662; 610; 766; 675	3,621; 3,536; 4,101; 3,256
7	1,290; 924; 1480; 898	5,438; 4,224; 4,380; 5,132
14	1,777; 1,522; 748; 1,575	10,567; 4,242; 9,795; 6,370
21	1,895, 663, 2,089, 2,251	12,466; 5,460; 12,317; 8,942
28	3,040; 3,232; 609; 1,365	5,366; 13,228; 5,319; 5,231
35	707; 1,293; 1,813; 2,023	11,097; 6,227; 6,451; 13,696
Depuration		
36	2,191, 2,568, 983, 1,382	6,560; 15,596; 10,744; 11,958
38	430; 619; 340; 329	5,461; 1,293; 3,613; 9,429
42	243; 38.8; 114; 65.0	451; 727; 7,208; 6,986
45	47.6; 49.4; 56.2; 35.2	1,658; 739; 718; 514
49	56.1; 1,104; 36.9; 27.5	126; 171; 182; 7,132
56	559; 19.1; 44,0; 154	169; 144; 106; 1630

Note: a) Values represent four replicates at each sampling point. <LOQ = below the limit of quantification.

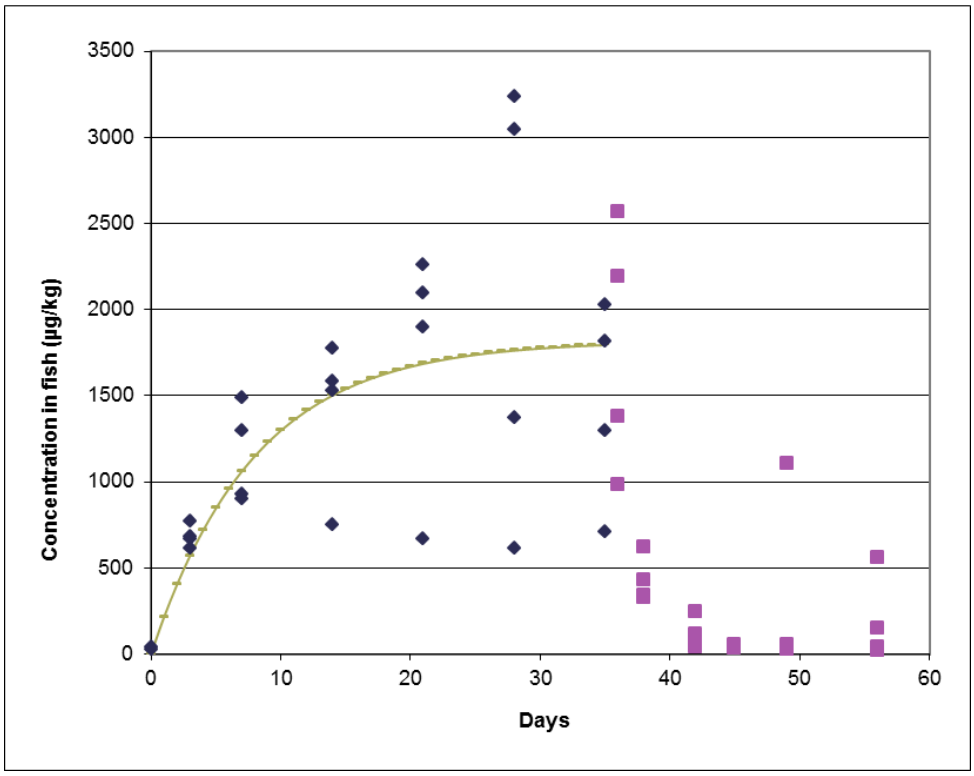


Figure 5: Plot showing the fish bioconcentration data for the 0.43 µg/l treatment group

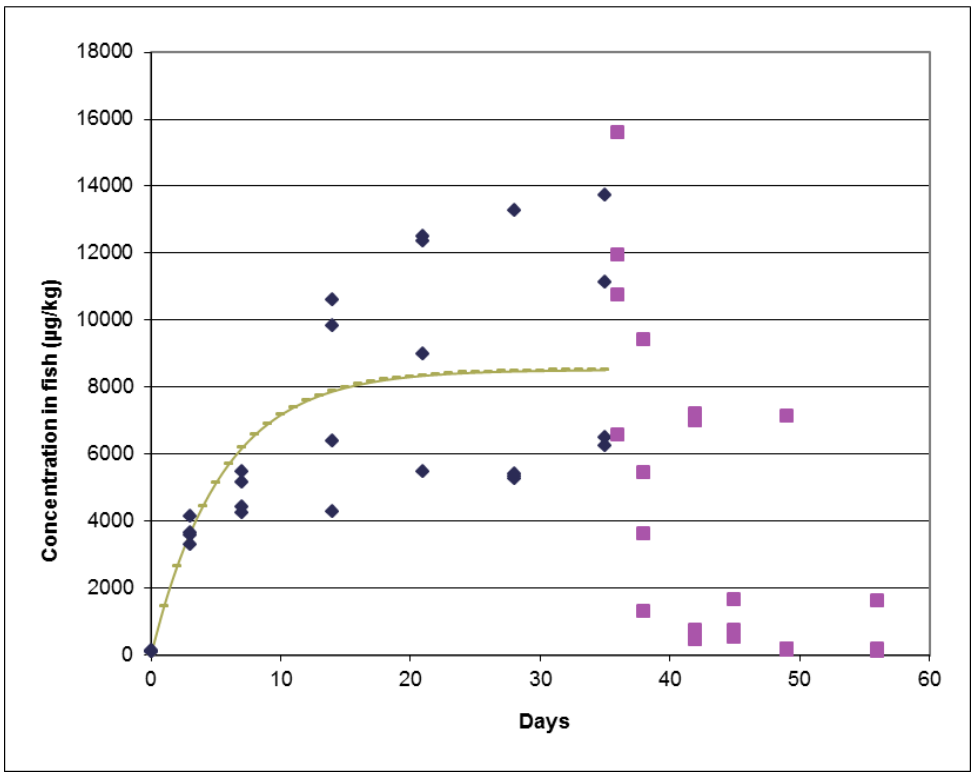


Figure 6: Plot showing the fish bioconcentration data for the 5.3 µg/l treatment group

0.43 µg/l treatment group

k_2 = 0.125 d^{-1} (see Figure 5). The R^2 value of the regression plot was relatively low (0.32) but the slope of the plot was statistically significantly different from zero ($p<0.05$). The standard error in the k_2 value was ±0.039 d^{-1}.

The value of k_1, obtained from least squares fitting of the uptake curve[14], was 529 l kg^{-1} d^{-1}, resulting in a kinetic BCF of 4,225 l/kg. Lipid normalisation of this value results in a BCF of 7,540 l/kg. These values are very similar to those reported in the registration dossier obtained by the simultaneous method.

5.3 µg/l treatment group

k_2 = 0.184 d^{-1} (see Figure 6). The R^2 value of the regression plot was 0.57 and the slope of the plot was statistically significantly different from zero ($p<0.05$). The standard error in the k_2 value was ±0.034 d^{-1}.

The value of k_1 obtained from least squares fitting of the uptake curve was 296 kg^{-1} d^{-1}, resulting in a kinetic BCF of 1,607 l/kg. Lipid normalisation of this value results in a BCF_L of 2,870 l/kg. Again, these values are similar to those reported in the registration dossier obtained by the simultaneous method.

Overall, broadly similar values for the kinetic BCF are obtained using both the simultaneous method and the sequential method for estimating k_1 and k_2.

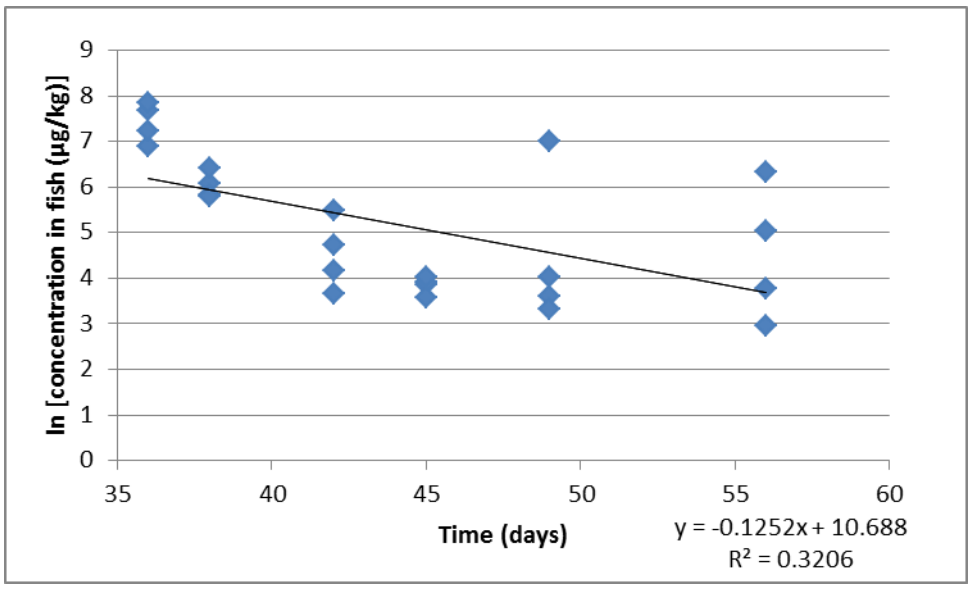


Figure 7:Plot of ln [concentration in fish] versus time for the 0.43 µg/l treatment group

[14] The eMSCA does not currently have access to the necessary software to estimate the uncertainty in this value.

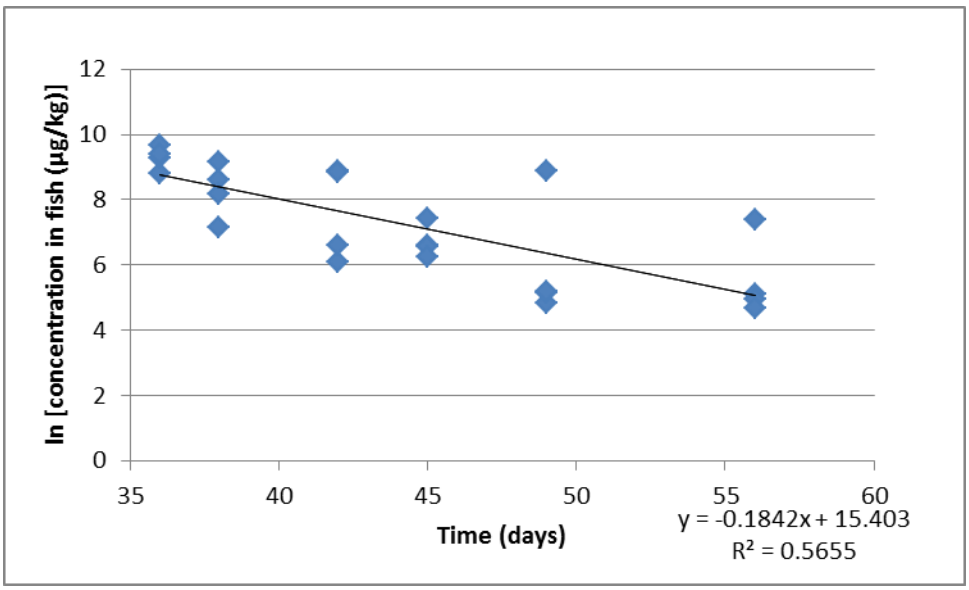


Figure 8: Plot of ln [concentration in fish] versus time for the 5.3 µg/l treatment group

No information on the growth of the fish during the test is given in the registration dossier. It is therefore not possible to determine if a correction for growth dilution is appropriate in this study.
Overall, although there is some uncertainty to this study resulting from the variability in the data at some time points, the results show that L4 has a BCF value >5,000 l/kg at the lower exposure concentration when lipid normalised. The BCF measured at the higher exposure concentration is <5,000 but >2,000 l/kg when lipid normalised. The lower BCF at the higher exposure concentration may indicate that the bioavailability of L4 in this test was limited. The test concentration of 5.3 µg/l was close to the water solubility of L4 (6.7 µg/l). Therefore, in the opinion of the eMSCA, the values obtained at 0.43 µg/l give a more realistic indication on the bioaccumulation potential of L4 than the values obtained at 5.3 µg/l. Thus, it is concluded that the lipid normalised BCF_L for L4 is in the range 6,840-7,540 l/kg, depending on the method used to calculate the BCF from the experimental data.

Although the BCF value is relatively high for L4, the substance also depurates reasonably rapidly from the fish (as evidenced by the fact that the k_2 value is around 0.124-0.211 d^{-1}), giving a clearance half-life of between 3.3 and 6 days. Brooke and Crookes (2012) concluded that substances with a k_2 over around 0.15 day^{-1} would not be expected to exhibit a BCF above 2,000 l/kg. The k_2 values determined for L4 straddle this value and so are, at the lower end of the range, consistent with a BCF of >2,000 l/kg. It is possible that the k_2 value may depend on the lipid content of the fish (Brooke and Crookes, 2012) and could potentially be smaller in fish with higher lipid contents.

The fish lipids declined slightly during the test. The mean lipid contents were 3.4% at the start of the test, 2.8% on day 35 and 2.1% on day 63. There was no statistically significant difference between the mean lipid contents at the start of the test and those at day 35 and 63, nor between those at day 35 and day 63 ($p>0.05$). The mean lipids represent those in the controls and exposed groups combined (two fish from each group were sampled at each time point).

7.7.3.1.2. Dietary study

A dietary bioaccumulation test using the OECD 305 methodology and performed according to GLP has been carried out with L4 (registration dossier, 2011). The test used a flow-through test system at 12°C. The test was performed on rainbow trout (*Oncorhynchus mykiss*). The fish had a mean weight of 0.85 g (range 0.51 to 1.1 g) and a mean length of 46 mm (range 42 to 50 mm) at the start of the test.
The test consisted of a 42-day uptake period followed by a 25 day depuration period (see below). The food used in the test consisted of 55% protein, 15% fat and 2% fibre.

Furthermore, the food was spiked with the test substance to a nominal concentration of 500 µg/g. The concentration of the test substance was analysed prior to the start of the test and on days 14 and 42 of the uptake period. The feeding rate used in the test was 3% of the body weight per day; the ration of food was adjusted based on the wet weight of the previous group of fish sampled.

The test was carried out in duplicate with three fish being sampled from each test chamber and control chamber on days 1, 3, 7, 10, 14, 21, 28, 35[15] and 42 of the uptake phase and days 1, 3, 7 and 14 of depuration.

Parent compound analysis of the L4 concentration was carried out by GC-MS. In addition, an HPLC/RAD method was used on depuration day 1 in order to identify any ^{14}C-containing metabolites present in the fish. The lipid contents of the fish and feed were determined prior to the start of the test, on days 10 and 42 of uptake and at test termination.
The dissolved oxygen concentration during the test was ≥4.7 mg/l (≥45% of saturation) (up to the power outage on day 25 of depuration; see Figure 10). Although this is relatively low it was considered in the test report that this did not affect the results of the test as no mortalities or sub lethal effects occurred up to the power outage. However, one of the validity criteria of the OECD 305 test is that the dissolved oxygen concentration should remain ≥60% throughout the study. This is discussed further below.

The mean concentration of the test substance in the feed was 534 µg/g and the concentration in food was found to be homogenous and stable over the duration of the uptake period. The mean (±standard deviation) lipid content of the food was 17.7±0.68%. The time weighted average lipid content (±standard deviation) of the fish was 5.93±1.69%.

Steady state was not reached by day 42 of the uptake as the mean concentrations on days 28, 35 and 42 were statistically significantly different ($p \leq 0.05$). However, the day 42 concentrations were to estimate an “apparent” steady-state BMF. The mean concentration of L4 in fish on day 42 was 78.0 µg/g based on parent compound analysis. Furthermore ^{14}C-analysis indicated that 91.6-102% of the radioactivity present was as parent compound with no identifiable metabolites present. Based on the day 42 concentration the “apparent” steady state BMF was estimated in the test report as 0.15 (not lipid normalised) or 0.44 (lipid normalised; using the time weighted average lipid content of the fish).

The kinetic BMF estimated was 3.8 (growth-corrected and lipid normalised, using the time weighted average lipid concentration).

It is important to note that there are some limitations to the study. These include the following:

- The fish concentrations are reported as whole fish concentrations minus digestive tract during the uptake phase and whole fish minus the digestive tract and liver during the depuration phase. Removal of the digestive tract prior to analysis is compatible with the OECD 305 test guideline as it avoids potential complications from the presence of undigested food. However, the effect of removal of the liver prior to analysis is unclear.
- The dissolved oxygen fell below 60% of saturation (<6.3 mg/l at 12°C) on several occasions during the study. This is one of the validity criteria in the OECD 305 test guideline. Although there were no obvious signs of stress in the fish prior to the malfunction, it cannot be ruled out that the low dissolved oxygen concentrations affected the validity of the study. Further, due to the abrupt termination of the study on day 67, it is not clear that the depuration phase was long enough to reach an appropriate reduction in body burden.

Overall, the study shows that the lipid normalised and growth-corrected BMF for L4 is above 1 and a BMF value 3.8 was estimated. However, the validity of the study is

[15] One of the samples on day 35 was accidently spilt and so only 5 fish were analysed for the treatment groups.

questionable as the dissolved oxygen concentration was low during a substantial part of the study, and it cannot be ruled out that the fish were stressed during the study. The importance of this in terms of the overall results from the study cannot be ascertained.

7.7.3.1.3. Other information

The Registrant(s) cite the ECHA PBT guidance (R11) suggesting that valid BCF values may not be possible for low solubility chemical from aqueous fish bioconcentration studies due the difficulty in maintaining test substance concentration. In response the eMSCA notes that there is no indication there was a problem in maintaining the exposure of L4. R11 also states that the aqueous test *may still be applied to strongly hydrophobic substances (having log Kow >6.0) if a stable and fully dissolved concentration of the test substance can be maintained in the water*.

The Registrant(s) state that steady state may be difficult to achieve for highly lipophilic and adsorbing substances. However, the robust study summary (RSS) in the registration dossier states that steady state was reached at day 14 for both test concentrations. The Registrant(s) explain that this is because the subsequent fish concentrations measured after that time were not statistically different. Therefore, reaching steady state does not appear to be an issue for the L4 study. In any case, as a kinetic BCFs have been derived (both significantly exceeding 5000), achievement of steady state is not essential to reach a conclusion in this case.

In their PBT assessment, the Registrant(s) consider that the depuration rate constant from the fish bioconcentration test carries the most weight for the bioaccumulation assessment. They argue that these are more reliable metrics as they are *independent of the exposure concentration and route of exposure*. The eMSCA is unclear why these issues are a concern in this instance, and highlight that the REACH Annex XIII criteria specify a BCF value exceeding 2000 or 5000.

Therefore, while a depuration half-life might be useful when a valid BCF value is not available, where the half-life information comes from that test, in the view of the eMSCA the BCF value is the result that should be taken from the test for comparison with the REACH Annex XIII criteria. The eMSCA would agree that interpreting a fish dietary study with respect to the REACH Annex XIII criteria is more challenging, and note that the OECD guidance for this test does tentatively suggest the use of the k2 value for used in PBT assessment. This is described in more detail below.

The Registrant(s) argues that the half-life in the fish in the test is <70 days which according to Goss et al. (2013) is indicative of a chemical that is not bioaccumulative. The eMSCA disagrees with this, principally as the value derived by Goss et al. (2013) is not animal specific. Different taxa have markedly different rates of metabolic capacity, and so it is not appropriate to derive a single half-life applicable across all species. In the MSC opinion (ECHA, 2018) for the P and B assessment of D4 and D5, the value cited by Goss et al. (2013) was considered not to account of a number of sources of variation in elimination half-lives. For example, due to the sizes of different organisms, species, lipid content, metabolism. Other complications were cited as growth and reproductive activity. When the assumptions used to derive the 70-d value were analysed it was shown that the BMF could exceed one when the elimination half-life was as short as 7.7 days when the conditions more closely mirrored the fish dietary bioaccumulation test guideline (for example uptake is greater due to a higher feeding rate than assumed by Goss et al. (2013), and food lipid content is greater than the standard lipid content of the fish).

The MSC opinion also highlights that the kinetic process of bioconcentration are dependent on the fish size as the uptake rate constant can vary with size, the corresponding depuration rate constant will be higher or lower to achieve the same BCF value. A comparison of the depuration rate constant in fish bioconcentration tests to the measured fish BCF value is described in report published by the UK Environment Agency (Brooke and Crookes, 2012) and cited in the OECD guidance for the OECD 305 Bioaccumulation test method. The analysis indicates that a (lipid normalised) k2 value below 0.085 d^{-1} (i.e. 8.2 days) is comparable to a BCF exceeding 5000. This is considerably shorter than the 70 days ascribed to Goss. The eMSCA appreciates that there is some uncertainty in the

analysis, for instance it does not account for different fish species, and reflects only the ~150 chemicals in the dataset. Therefore, it would be used as part of weight of evidence.

However, the eMSCA does note that the k2 calculated in the fish feeding study is 0.012 d^{-1}, suggesting BCF >5000, when considering the OECD guidance, or when the Goss et al. (2013) calculations are amended to account for the feeding rate.

7.7.3.1.4. Fugacity ratios

The Registrant(s) also determined fugacity ratios for L4 based on the measured log Kow (8.21) and BCF values (steady state and kinetic for each concentration). F/Rs are an approach for comparing laboratory and field measures of bioaccumulation. The approach expresses bioaccumulation metrics in terms of the equilibrium status of the chemical, with respect to a reference phase. Differences in numerical scales and units are eliminated by converting the data to dimensionless fugacity (or concentration-normalized) ratios. Fugacity ratios greater than 1 indicate an increase in chemical thermodynamic activity in organisms with respect to a reference phase (e.g. biomagnification). Fugacity ratios less than 1 indicate a decrease in chemical thermodynamic activity in organisms with respect to a reference phase (e.g. biodilution) (Burkhard et al., 2012). These are in the region of 3E-04 to 8E-04 for L4, which the Registrant(s) state as indicating the chemical in the organism is at a lower fugacity (or chemical activity) than in the water. The Registrant(s) states the value of the ratios suggests that either uptake may be less than expected or alternatively elimination is faster than might be expected based on lipophilicity. The discussion notes that n-octanol and lipid are assumed to be equivalent, and work using olive oil is in progress to determine lipid-water partitioning for siloxanes. Finally, it notes that the calculated fugacity ratios should be used with caution at this stage.

The Registrant(s) also determined fugacity ratios (F/R) for L3 based on the measured log Kow (6.6) and BCF values (steady state and kinetic for each concentration). These are in the region of 0.06 to 0.13. The Registrant(s) states that this indicates that the chemical is at a lower fugacity (or chemical activity) in the organism than in the water. The Registrant(s) state that the value of the ratios suggests that either the uptake may be less than expected or alternatively that the elimination is faster than might be expected based on lipophilicity. The discussion notes that n-octanol and lipid are assumed to be equivalent, and work using olive oil is in progress to determine Klipid-water partitioning for siloxanes. Finally, it notes that the *calculated fugacity ratios presented should be used with caution at this stage*.

The eMSCA notes that there is not yet acceptance of fugacity ratios by regulators for REACH. The Registrant(s) highlight one of the issues, which is the assumption of lipid partitioning being equal to octanol/water partitioning. This is not yet resolved. There is also no accepted standard method for deriving the ratios
The F/R value is also sensitive to the log Kow value (inversely affected). For L4, the high log Kow value (8.21, OECD 123) is a further reason that the F/R value is very small. It is arguable that a QSAR would also suggest relatively low BCF based on the log Kow value. However, this is at odds with the measured fish data which indicates high levels of accumulation.

The eMSCA notes that substances with a high BCF may well have F/R <1 for biota water. This is because the theoretical maximum fugacity ratio for biota/water for water exposure alone is 1. Therefore, using a BCF test in the F/R calculation alone will not provide a full indication of biomagnification potential.

The eMSCA notes that in the case of another siloxane (D5), the fish BCF values exceeded 5000, BMF and TMF values exceeded 1, and yet the F/R <1. This suggests that F/R may not be a robust guide for the fish BCF value or REACH “B” assessment.

Overall, while the eMSCA appreciates the theoretical outcome of the F/R calculation, the available measured data in whole animals should be preferred. In this case the (lipid normalised) BCF values of up to 6000 are in contrast to the low levels of accumulation that are suggested by the fugacity ratios.

The Registrant(s) have provided a presentation (Huggett et al., 2015) assessing *in vitro* hepatic transformation of (radiolabelled) D5 and L4 in a number of animals: rainbow trout, carp, catfish, kestrel, quail, rat, mink and human.

Biotransformation was conducted in triplicate using 10 ml vials. These were stoppered, and placed in a shaking water bath. Quail, kestrel, rat and human were run at 37 °C, catfish and carp at 25 °C, and trout at 16 °C. The temperature of mink is not specified, but the eMSCA assumes this was also 25 °C . The test was run for an hour, with vials also sampled at 0, 15, 30 and 60 minutes. A Fluroxypry positive control as well as (heat) deactivated and control (without test substance) were also run. The poster indicates that the analytes remained in solution when the hepatic matrix was introduced, but were rapidly lost in the controls. It is not clear if this refers to volatilisation or hydrolysis. The results are summarised in Table 28 below. HPLC/β-RAM was used for analysis.

Table 28: Percentage loss for radiolabelled D5 and L4 in microsomes from multiple species

	D5		L4	
	% Recovery[a] at 60 minutes	% Loss at 60 minutes	% Recovery[a] at 60 minutes	% Loss at 60 minutes
Mink	82.24	10.89	78.64	18.47
Quail	92.86	0.54	91.79	1.79
Carp	92.04	0.67	93.97	1.56
Trout	91.29	1.12	89.73	6.83
Kestrel	91.60	0.74	No result	
Rat	88.16	4.67	92.01	2.59
Human	87.58	5.95	90.08	5.37
Catfish	90.91	1.55	91.94	0.58

[a] The eMSCA assumes this is total radioactivity

Hugget et al 2015 concludes that the results show greatest potential for siloxane biotransformation in mink (≥12%), but negligible ability for transformation was shown by quail, kestrel, carp and catfish. Trout, rat and human demonstrated some ability to transform both substances. Biotransformation products were noted to be more polar than the parent substances in the radiochromatogrames but not identified. The positive control indicated that the systems were functioning correctly as fluroxypyr was degraded within 60 minutes (below detection limit).

The eMSCA notes that only a qualitative interpretation is possible, however without any benchmark interpretation is only possible relative to the different species in the test. On this basis the eMSCA would agree that rat, mink and humans appear to have greatest metabolism exhibited. However, the trout result for L4 is an outlier and out of line with the other data. The variability/ repeatability of the test is unknown. For instance, the eMSCA notes that while the S9 (Johanning et al., 2012) also uses three replicates, the test is run until 120 minutes with additional sampling at 90 and 120 minutes.

Even then it is difficult to interpret the study for the real environment without knowledge of the whole animal ability to transform the substances (it is appreciated that this is ethically difficult). The eMSCA notes that metabolism does occur in the fish bioaccumulation study for L4, however the BCF value still exceeds 5000.

Fluroxypry has a quoted BCF value of 62.1 (species not known)[16], by comparison L4 has a BCF in the range 6,840-7,540 l/kg (fathead minnow) and D5 has a BCF in the range 10,550 – 11,048 L/kg (common carp) or 7,060 L/kg (fathead minnow).

[16] http://sitem.herts.ac.uk/aeru/ppdb/en/Reports/347.htm

The eMSCA notes that for D5, S9 studies have derived a Km which exceeds the measured k2 value in whole fish bioaccumulation tests. As the k2 accounts for metabolism and other processes (for example excretion) it is not feasible that the km can exceed the k2 in whole fish. This therefore suggests km was over-estimated in the S9 test. If this also occurs in experiments with other microsomes, it suggests caution should be exercised in interpreting the results.

7.7.3.2. Bioaccumulation in terrestrial organisms (soil dwelling organisms, vertebrates)

No data on bioaccumulation in terrestrial organisms are available in the registration dossier.

7.7.3.3. Summary of bioaccumulation

L4 has a log Kow of 8.21 and therefore screens as B and vB. In a fish bioconcentration test using fathead minnow (*Pimephales promelas)*, lipid normalised (5%) values for the two concentrations tested were between 6,840-7,540 l/kg for the lower concentration, and between 2,870 and 3,140 l/kg for the higher concentration. The higher concentration (5.3 µg/l) is very close to the water solubility limit of L4, therefore the lower BCF at this treatment could suggest that bioavailability was limited when normalised to a 5% lipid content.

Results of a dietary bioaccumulation study using rainbow trout (*Oncorhynchus mykiss*) are also available for L4, which shows that the lipid normalised and growth-corrected BMF for L4 is 3.8 . The results support the findings of the BCF study, although the eMSCA has some concerns about the validity of the dietary study due to an issue with the oxygen supply to the fish.

7.7.4. Environmental monitoring data

In a compilation of Norwegian monitoring from 2002 – 2012[17] (Arp, 2012), L4 was detected more frequently that L2 and L3, but less than the cyclic siloxanes D4-D6. L4 was not detected above the l.o.d. in fresh/marine water, nor freshwater sediment (7 and 3 samples respectively), but was in marine sediment, WWTP sludge and water, (11 samples, 4 detections - max 29 ng/g dw; 3 samples, 3 detections, max 95 ng/g dw, 5 samples, 1 detection 15 ng/l) from monitoring performed in 2005 and 2007. A number of biota were also sampled: Cod liver (21 samples, 5 samples above the l.o.d. max 2.85 ng/g ww), Polar Cod fillet (4 samples, no detections), Blue Mussels (2 samples, no detections), bird liver (14 samples, no detections). These were different studies conducted in 2007 and 2009. L5 was analysed in the same biota samples as L4. It was only detected in 3 fish liver samples (maximum concentration 1.46 ng/g ww). The frequency of detection of L5 in the remaining environmental matrices was similar to L4, although the detections in marine sediment (max 55 ng/g dw), STP sludge (400 ng/g dw) and STP water (35 ng/l) were at higher concentrations. L3 was detected in fish liver (4 samples, max 0.33 ng/g), but not the remaining biota. A similar detection pattern in the environmental matrices was also seen, with detection in 3 STP sludge samples (max 31 ng/g dw), and 1 STP water sample (32 ng/l), although not in marine sediment.

The Norwegian Environment Agency has since performed more environmental monitoring projects that included L4. In samples collected in 2016, the linear siloxanes were detected in all samples of indoor air, house dust and sewage sludge. L4 was detected in all samples of surface water (3.7 – 24 ng/L) leachate water (2.4 – 3.1 ng/L), sewage sludge 16-33 ng/g), house dust (0.17 – 1.6 ng/m^3) and indoor air (1.1–37 ng/m^3), but not in samples

[17] This includes data from a further citation: SCHLABACH, M., ANDERSEN, M. S., GREEN, N., SCHØYEN, M. & KAJ, L. 2007. Siloxanes in the Environment of the Inner Oslofjord. *NILU OR,* 27**,** 2007.

from rat and brown trout. The measured concentrations were below the predicted no-effect levels and the authors expressed that they expected the exposure via environmental pathways to be much lower compared to the exposure via use of cosmetics/personal care products (Schlabach et al., 2017). The following year, another campaign found L4 in inlet wastewater and landfill runoff (COWI 2018) in samples from 2017.

In samples collected in 2018, the linear siloxanes were detected in all selected sample types, including indoor environments . L4 was found in almost all samples of sewage water (3.3 – 58 ng/L) and house dust (1.0 – 152 ng/m^3). L4 was also detected in gull eggs (3.1 ng/g), blue mussels (0.35 ng/g) and sediments (0.15 – 1.0 ng/g), albeit at lower detection frequencies and levels of L4 compared to L5 (Schlabach et al., 2019).

Evenset et al. (2009) sampled sediment and biota in a number of locations in the Norwegian Arctic in 2004 and 2008. L4 and L5 were not detected at the three locations sampled for sediment. This was similar to other linear and cyclic siloxanes. Fish liver from Atlantic cod and Polar cod were sampled at three locations and whole Polar cod at one further location. L4 and L5 were not detected in any fish (LOD appears to be between 0.15 – 0.75 ng/g ww). L3 was detected in two liver samples, and the cyclic siloxanes were detected in nearly all samples. The samples taken in 2004 were not analysed until 2008.

The Swedish Environmental Research Institute performed a national screening programme of different media for siloxanes in 2004 (Kaj et al., 2005b). This contained two parts, firstly a national programme with sites designated as “background”, “potential point” and “diffuse” sources. Matrices sampled were air, sediment, water, sludge and biota. Secondly a regional screening programme covering sites in thirteen regions with STP “water”, sludge, sediment and fish sampled. Both programmes analysed for D4, D5, D6, L2, L3, L4 and L5. L3, L4 and L5 were not detected in any of the background samples (3 air, 3 sediment and 3 biota). L3 was not detected in any point or diffuse sources. L4 and L5 were both detected in sediment samples (L4: ¼: 0.9 ng/g dw; L5 2/4: 0.7 and 1.7 ng/g dw) from point sources. Both L4 and L5 were also detected in the three sludge samples from diffuse sources (8 – 16 and 24 – 46 ng/g dw respectively). In the regional screening, L4 and L5 were not detected in STP water or fish (muscle) samples. L4 was detected in 43 out of 51 municipal sewage treatment plants, in one sediment sample, and detected in 2 out of 39 breast milk samples (0.008 and 0.013 µg/l). L5 was detected in 42 out of 51 regional sludge samples and 3 sediment samples. It was not detected in any of the 39 breast milk samples (l.o.d. 0.04 µg/l). Overall, concentrations of the linear siloxanes were much lower than for the cyclic siloxanes, in some cases for D5 by up to three orders of magnitude. L3 was not detected in any sediment or STP water samples but was detected in 12 sludge samples, and 6 breast milk samples (0.003 – 0.008 µg/l).

Kaj et al. (2005a) also conducted a wider analysis of siloxanes in the Nordic countries. This included monitoring of air (24, l.o.d. 0.006 ug/m^3), soil (2, 0.1 ng/g dw), water (13), sediment (24, variable l.o.d. generally <1 ng/g dw), WWTP/landfill effluent (23, variable l.o.d. generally <0.001 ug/l), WWTP sludge (14, ng/g dw), and biota. Biota consisted of composite samples of livers of different fish species (21), seabird eggs (17), and blubber of cetaceans (7). L4 was not detected in air, soil or water samples. However, it was detected in the remaining media. L4 was detected in all WWTP sludge samples (range 1-450 ng/g dw), a small number of sediment samples (<l.o.d – 29 ng/g dw), and some industrial effluent. It was detected in one biota sample (fish liver, 1.1 ng/g ww), which was notable for also containing high levels of D5 (around 100 times those of D5 in other samples). L5 was not detected in any air sample, nor natural waters or the two soil samples. It was detected in all sewage sludge samples 3 – 550 ng/g, and some landfill and STP influents and one STP effluent (<l.o.d – 0.041 µg/l). It was not detected in any of the biota. L3 was not detected in any of the biota, air, sediment or natural waters. It was detected in two of the STP influents (0.0034 – 0.014 µg/l).

As part of routine monitoring, predatory fish (Lake Trout, *Salvelinus namacycush*, or Walleye, *Sander vitreus* where Lake Trout were not present) were collected by Environment Canada across 16 Canadian water bodies in 2009 and 2010 (McGoldrick et al., 2014). L4 was not detected in any of the 87 fish caught (detection limit, DL, 0.31 ng/g w/w), and

neither were L2 (L2, DL 0.30 ng/g w/w) or L3 (DL 0.42 ng/g w/w). L5 was detected in one sample (DL 0.27 ng/g w/w). In contrast the cyclic siloxanes D4, D5 and D6 were detected in all samples (0.60, 0.50, 0.37 ng/g w/w respectively).

Sanchís et al. (2015b) have reported detecting both cyclic and linear VMS in different media at the Antarctic. L4 was detected in soil (range below l.o.d. – 602 pg/g dw, 11 samples) and phytoplankton (range below l.o.d. – 17 pg/g dw, 11 samples), but was not detected in vegetation or Krill samples (17 and 11 samples respectively). The findings for L4 were generally consistent with the detection of L5 and L6, but L3 was also detected in Krill. In contrast, the cyclic siloxanes were detected in all of the media sampled, and often at concentrations up to 100 times greater than the linear siloxanes. The concentrations of cyclic VMS in phytoplankton were found to be negatively correlated with sea surface salinity, and Sanchís considered this to indicate a possible source from ice and snow melting. The cyclic siloxanes are the main focus of the discussion in the paper, principally as they are detected at higher concentrations than the linear homologues. The findings of this paper have been questioned (Mackay et al. 2015; Warner et al., 2015). One of the main concerns raised with the study was the possibility of contamination of the samples during collection and analysis, owing to inadequate sampling and storage procedures. Although Sanchís et al. (2015a) replied to these comments, some of the concerns raised by Mackay et al. (2015) and Warner et al. (2015) do appear to be legitimate and so the data are not considered further here.

Zhang et al. (2011) conducted monitoring of siloxanes, including L4 and L5, in the sediment of the Songhua River, and sewage sludge from eight WWTPs in the north east of China. The area sampled includes locations downstream of large and small cities, and a major silicone production site. 25 sediment samples and one sample from each WWTP were collected. Limits of detection for L4 and L5 were 0.86 and 0.35 ng/g dw, respectively, and appears to be both sediment and sludge). The paper does not provide specific concentrations of L4 and L5, but notes that these were “rarely detected in sediments”. Neither were detected above the l.o.d. in sewage sludge.

L4 has recently been detected in sewage sludge in Norway (Blytt and Stang, 2018). In 70 sludge samples collected across a total of 10 STPs, L4 was detected in 53 of the samples. The range of concentration was below l.o.d (0.010 mg/kg) to 0.11 mg/kg, but with an increasing trend. L3 and L5 were also monitored, together with other cyclic siloxanes. In a similar campaign from 2013, L4 was also detected, but with lower frequency and slightly lower concentrations (Blytt et al., 2013)

Lee et al. (2014) sampled sludge from 40 domestic, mixed and industrial wastewater treatment plants in Korea in 2011 for linear and cyclic siloxanes. They found much higher concentrations of the cyclic siloxanes compared to linear siloxanes. Concentrations of specific linear siloxanes are not provided in the paper (or in the supplementary information), only a summed total. Based on relative load graphs in the article, the longer chain lengths were detected (L10 was the most prominent), but the shorter chains, including L4, appear to have been at or around the detection limit. The researchers also noted that higher siloxane concentrations occurred in domestic WWTPs compared to the industrial plants.

Wang et al. (2015) conducted 7-consecutive-day monitoring of influent, effluent and sludge of a WWTP receiving domestic and food processing waste in China in 2014. L3, L4 and L5 were all below their detection limit (0.082, 0.09 and 0.091 µg/l) in the influent and effluent. In the sludge, L3 was below the detection limit (0.113 µg/kg) but both L4 and L5 were detected in all samples (1.27 – 92.9 and 33 – 164 µg/kg respectively). Similar to other studies, concentrations of the cyclic siloxanes were significantly higher.

Olofsson et al. (2012) reviewed trends of L3, L4 and L5 in Swedish sewage sludge between 2004 and 2010. Ten WWTPs receiving a mixture of effluent (large cities, medium cities, mixed domestic and industrial, and domestic) were sampled in the autumn of each year. L3, L4 and L5 were sampled in 6 or 7 of the years, with between 49 and 54 samples being taken in total for each of the three substances. The paper provides median concentrations

of 17, 57 and 240 µg/kg dw for L3, L4 and L5 respectively, with stated increases in concentrations of 28, 34, 26% over the period of sampling. More detailed data, such as the range of concentrations, is not provided in the paper, although the supplementary data does provide a graphical illustration. The total median concentration for all the siloxanes, including D4, D5 and D6, was 13500 µg/kg dw.

Bletsou et al. (2013) conducted monitoring of a single WWTP in Athens, Greece. The plant is indicated to serve 3,700,000 people. Samples of influent, effluent and sludge were collected over seven consecutive days in April 2012. L4 was detected in 6 out of 7 influent samples (<l.o.d. – 0.148 µg/l), 6 out of 7 effluent samples (<l.o.d. – 0.099 µg/l), and all seven sludge samples (0.050 - 0.063 mg/kg). L3 was not detected in the 7 influent and effluent samples, but was detected in the sludge (0.16 – 0.26 mg/kg). L5 was detected in all influent (0.010 – 0.067 ug/l) and effluent samples (0.0007 -0.012 ug/l), and sludge (0.21 -0.25 mg/kg). The eMSCA has been unable to obtain the supplementary information detailing the l.o.d.

Liu et al. (2014) investigated the occurrence of seven musks and seventeen siloxanes at 42 wastewater treatment plants across 23 cities in China from samples of anaerobic digested sludge after the dewatering process. Site predominantly received a mixture of domestic and industrial effluent, although a few received either exclusively domestic or industrial effluent. The l.o.q. for L3, L4 and L5 were 0.5, 0.6 and 0.7 ng/g of sludge. The concentrations of L3, L4 and L5 are not reported. By eye, the log Box & Whisker plots suggest L4 was not detected above the l.o.q. while L3 and L5 ranged from the l.o.q. to ~800 and 90 ng/g respectively, with medians of 20 and l.o.q. Cyclic siloxanes (D4, 5 and 6) were reported to account for 68% of the siloxanes detected, while L11-16 accounted for 84% of the linear siloxanes.

Xu et al. (2013) investigated the occurrence and fate of four cyclic (D3-6) and two linear siloxanes (L3 and L4) at a municipal WWTP in Beijing, China. The plant has a capacity of 400000 m^3/day, although it is not clear from the article what proportion is domestic and industrial. Water and sludge were collected from thirteen different points in the works on two occasions (January and April 2011). L3 was not detected in any sample and L4 in only one sludge sample and two aqueous samples (method detection limits 3.5 and 3.2 ng/l, and <1.0 and <1.0 ng/l respectively). In contrast D4, D5 and D6 were detected in all samples, and D3 in the majority of samples.

Sanchís et al. (2013) tested a new analytical method by sampling WWTP influent and effluent, river and sediment in northeast Spain. 15 influent and 16 effluent samples were taken from 17 WWTP as integrated samples over 24 hours in February 2011. One of these was also additionally sampled over one week in June 2011. Three aqueous and six sediment samples from two rivers were also collected in the February. All WWTPs appear to receive effluent from at least 135,000 people, and the level of treatment varied with some suites also having tertiary treatment or nitrogen and/or phosphate removal.

L4 was above the MloQ in seven and detectable but not quantifiable in a further three. Neither L3 or L4 were above the method MLoQ in the effluent, but detectable but not quantifiable in a further three and eleven samples respectively. L5 was above the limit in five and detectable but not quantifiable in the remainder apart from one sample. By contrast, for example, D5 was detected in all effluent samples. For the river sampling L3 was detected in one site in both sediment and water, while L4 and L5 were detected at the same point but only in sediment. MLoQ was 1.2, 1.4 and 0.5 ng/l in wastewater, and 0.9, 0.6 and 1.8 ng/g in river sediment. MLoD was half the MLoQ for sediment, and approximately 20-33% for wastewater. The river water MloQ is not discussed in the paper or supplementary information.

Ratola and co-workers have reported initial findings of cyclic and linear siloxanes at several locations in Portugal (Ratola et al., 2016). They sampled pine needles, soils and air (using

SIP[18] disks) across eight sites in Portugal covering urban, industrial, rural/remote, industrial, beach locations and a WWTP for four cyclic siloxanes (D3, D4, D5 and D6), four linear siloxanes (L2, L3, L4 and L5) and a silane in winter and summer. The use of pine needles built on a previous project to use them as biomonitors of airborne persistent organic pollutants. Analytical recoveries across the three matrices were similar, but varied for the different chemical with recoveries of the more volatile siloxanes (for example L2 and D3) being lower than the less volatile ones (for example L5 and D6). At the time of the presentation only limited data were available for pine needles and soils for the winter time in Porto (actual sample type not specified). The linear siloxanes were detected at low concentration (<1 ng/g wet weight) or were not detected. Cyclic siloxanes were detected at higher concentrations in almost all samples.

Pelletiera et al (2021) studied the bioaccumulation of the cyclic siloxanes (D3 to D6) and linear siloxanes (L3 to L5) in a food web in the St. Lawrence River downstream of the effluent of the municipal wastewater treatment plant in Montreal, Canada (Pelletier et al. 2021). In all biotic samples from individuals feeding in the effluent plume cyclic siloxanes were detected and the linear siloxane L5 was also abundant in walleye and gull eggs. Sediment-biota accumulation factor (BSAF) have been calculated for total siloxanes (∑D3 to D6 and L3 to L5) showing values of 65.4, 27.8, 9.9 and 6.4 g dw/kg ww for walleye, northern pike, yellow perch and round goby respectively.

Summary

There are several observations of L4 in the environment. Where sewage sludge has been monitored L4 can generally be detected, albeit at ng/g levels. Given the use in cosmetics/personal care products and automotive care products and the lack of biodegradability, detection at STPs is expected. In recent screening campaigns in Norway L4 has also been detected in indoor air and house dust.

Generally, the levels detected for the linear siloxanes are significantly lower than for the cyclic siloxanes. It should be noted that there is a large difference in supply volume for linear siloxanes compared to the cyclic siloxanes. Although D4 and D5 are registered at much higher volumes than L4, several uses of D4 and D5 have been restricted. Increasing supply volume can be expected for L4 since it is an alternative for the restricted uses of D4 and D5. Therefore, higher concentrations of L4 in the environment can be expected in future.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

The available aquatic toxicity tests have generally been carried out using the highest test concentration possible (derived from a nominal exposure concentration of 6.7 µg/l, which represents the water solubility of L4 in water).

7.8.1.1. Fish

7.8.1.1.1. Short-term toxicity to fish

The short-term toxicity data to fish given in the registration dossier are summarized in Table 29. The substance is not acutely toxic to fish at concentrations up to the limit of solubility in the test medium.

Table 29: Summary short-term toxicity of L4 to fish

[18] Sorbent-impregnated polyurethane foam [disks]

Species	Value	Remarks	Reference
Oncorhynchus mykiss	96h-LC_{50} > 6.3 µg/l	OECD TG 203, reliability score 1. Measured concentration (nominal 6.7 µg/l)	Registration dossier (study report 2008)

7.8.1.1.2. Long-term toxicity to fish

The long-term toxicity data for fish are summarized in Table 30.

Table 30: Summary long-term toxicity of L4 to fish

Species	Value	Remarks	Reference
Rainbow Trout (*Oncorhynchus mykiss*)	60-d (post-hatch) NOEC ≥ 7.9 µg/l (limit of solubility)	Fish, Early-Life Stage Toxicity test (FELS) OECD TG 210. Flow through test, with results expressed as TWA concentrations. No effects for the following endpoints: hatching, larval survival abnormal appearance and behaviour.	Registration dossier (study report, 2013)[19]
Fathead minnow *(Pimephales promelas)*	35d-NOEC ≥ 5.3 µg/l	Results from OECD TG 305 bioconcentration test, reliability score 1. Endpoint mortality. Measured concentration (nominal 6.7 µg/l). As this was from a bioconcentration study not all relevant long-term endpoints (for example growth) were studied.	Registration dossier (study report 2006)

The results in the FELS test are quoted as time-weighted means. The highest concentration was nominally 6.7 µg/l (limit of water solubility), although the time-weighted mean for this treatment was 7.9 µg/l. This indicates that saturation was achieved or possibly very slightly exceeded. The RSS states that there were no statistically significant treatment related effects in any treatment, and the eMSCA agrees with this conclusion.

In the fish bioconcentration test using L4, the substance was not toxic to fish over longer-term exposure at concentrations up to the limit of solubility in the test medium. Sub-lethal endpoints such as adverse impacts on growth or potentially sensitive early life stages are not considered in a bioconcentration study.

This means this test alone cannot fulfil the chronic fish toxicity endpoint. However, the lack of effects in the measured endpoints are consistent with the FELS test.

7.8.1.2. Aquatic invertebrates

7.8.1.2.1. Short-term toxicity to aquatic invertebrates

No short-term toxicity data for invertebrates are included in the registration dossier. Testing for the endpoint is waived, as a long-term test result is available.

7.8.1.2.2. Long-term toxicity to aquatic invertebrates

The long-term toxicity data for aquatic invertebrates given in the registration dossier are summarized in Table 31. The substance is not toxic to aquatic invertebrates over longer-term exposure at concentrations up to the limit of solubility in the test medium.

Table 31: Summary long-term toxicity of L4 to aquatic invertebrates

Species	Value	Remarks	Reference
Daphnia magna	21d-NOEC ≥ 4.9 µg/l	OECD TG 211, reliability score 1. Endpoint reproduction. Measured concentration (nominal 6.7 µg/l)	Registration dossier (study report 2009)

The eMSCA notes that there is a deviation in the feeding regime for the 21-day *Daphnia* study guideline.

7.8.1.3. Algae and aquatic plants

The algal toxicity data given in the registration dossier are summarised in Table 32. The substance is not toxic to algae at concentrations up to the limit of solubility in the test medium.

Table 32: Summary long-term toxicity of L4 to algae

Species	Value	Remarks	Reference
Pseudokirchneriella subcapitata	72h-NOEC > 2.2 µg/l	OECD TG 201, reliability score 1. Endpoint growth rate. Measured concentration (nominal 6.7 µg/l)	Registration dossier, (study report 2008)

PNEC aquatic: No aquatic PNEC could be derived due to the lack of effects in the available tests, which include three chronic results.

7.8.1.4. Sediment organisms

The sediment toxicity studies performed for L4 are summarised in Table 33.

The registration dossier contains one study with the sediment organisms *Hyalella azteca*. No effects were seen on mortality, behaviour or dry weight of surviving organisms at concentrations up to 68 mg/kg dry weight (the highest concentration tested). Furthermore, in a registration update a *Lumbriculus variegatus* test performed according to OECD 225 and GLP using L4 has been included. This was conducted using natural sediment from the same source as the *Hyallela* study, albeit with a marginally different particle size distribution. No effects were observed in the study up to a maximum (mean measured) concentration of 17 mg/kg dw. Normalised to 5% organic carbon, this is 34 mg/kg dw. The concern is that this *Lumbriculus* test provided by the Registrant(s) does not test concentrations up to the "T" limit for L4. *Lumbriculus* were the most sensitive species for the L3 dataset and the endpoint has been read-across to L4 in the registration dossier.

Given the similar properties and structural similarities of L3 and L4 eMsCA considers it justified to read across sediment toxicity data from L3 to L4. No effects at the limit of solubility have been reported in short-term and long-term studies in other trophic levels conducted with both substances.

Table 33: Summary of toxicity of L4 to sediment organisms

Species	Value	Remarks	Reference
Hyalella azteca	28d-NOEC ≥68 mg/kg dry wt. 28d-LC_{50} >68 mg/kg dry wt.	Test to OPPTS Guideline 850.1735, reliability score 1. Endpoints survival, behaviour and dry weigh of surviving organisms. Measured concentration. Natural sediment.	Registration dossier (study report 2013),
Lumbriculus variegatus	28d-NOEC ≥ 17 mg/kg dry wt. 28d-EC_{50} >17 mg/kg dry wt.	OECD TG 225 (Sediment-Water *Lumbriculus* Toxicity Test Using Spiked Sediment), reliability score 1. Natural sediment (2.5 % OC). Endpoints survival and biomass.	Registration dossier (study report 2016),

The *Hyalella* test used natural sediment and eMSCA has made some comparisons of the matrix characteristics with artificial sediment:
The pH of the overlying water is not provided in the robust study summary, but is noted to be *above or below the water quality range*. The test guideline states that reconstituted water should have pH between 7.8 and 8.2. The pH of the sediment is stated to be 5.6, although a pH for this is not specified in the Hyallela guideline. The TG for Chironomids and *Lumbriculus* indicates the sediment pH should be above 6.5. It is not clear what effect pH outside of TG would have on results, although the Registrant(s) indicate that the pH of the overlying water was within the tolerance range of the animals and are not thought to affect the outcome of the study. Grain size is noted as influencing the bioavailability of the test substance in the endpoint guidance for sediment toxicity (ECHA, 2018).It can be seen that as well as the difference in particle type, the organic carbon content of the natural sediment is higher than the artificial sediment.

In the registration the Registrant(s) derives the PNEC for L4 from a read-across to L3 based on tests on *Chironomus riparius*. However, a newer study is available for L3 on *Lumbriculus variegatus* (study report 2017) resulting in a NOEC of 7.8 mg/kg dw. When normalising the NOEC of 7.8 mg/kg dw to 5% carbon content gives a NOEC of 18.6 mg/kg dw.

Applying an assessment factor of 10 this gives a of $PNEC_{sediment}$=1.86 mg/kg dw.

7.8.1.5. Other aquatic organisms

None.

7.8.2. Terrestrial compartment

Table 34: Summary of toxicity to soil macroorganisms

Species	Value	Remarks	Reference
Earthworm (*Eisenia fetida*)	NOEC (56-day) ≥ 1000 mg/kg	OECD 222, Earthworm reproduction test. 2019. Natural soil.	Registration dossier (study report 2019),

The registration dossier includes the results of an earthworm reproduction test using L4. The overall 56-d NOEC (nominal) from the study was 1000 mg/kg soil dw (mean measured NOEC 440 mg/kg soil dw). No effects on survival, reproduction or weight were observed. The Registrant(s) consider the study to be "reliable without restriction".

The test was conducted as a limit test at 1000 mg/kg (n=8), however two other concentrations were also tested: 10 and 100 mg/kg (n=1). Concentrations ranged from 43 to 51% of nominal concentrations at test initiation through day 28 and slightly declined over the last 4 weeks of the 56-day exposure period to a range of 32 to 33%. An overall

mean measured concentration was calculated to be 440 mg/kg (44% of nominal concentration).

A homogeneity and stability study was conducted in advance of the earthworm study. The homogeneity results indicate a uniform distribution of the substance in the soil column at the start of the experiment. The stability results indicate that the substance was not stable and sampling did not go beyond day 35. The chromatograms did not indicate the presence of degradation products, which, together with the steady loss of 14C activity, show that the primary mechanism of test article loss was volatilization of 14C-L4 from the simulated OECD 222 set-up.

Table 35: Summary of toxicity to soil microorganisms

Species	Value	Remarks	Reference
Soil microorganisms	EC50 (28 d) > 100 mg/kg soil dw	OECD TG 216. Soil Microorganisms: Nitrogen Transformation Test.	Registration dossier, (study report 2019)

The toxicity data for soil microorganisms given in the registration dossier is summarized in Table 35. The substance is not toxic to soil microorganisms over longer-term exposure at concentrations up to 100 mg/kg soil dw.

PNEC soil has not been derived due to lack of effects in the available tests.

7.8.3. Microbiological activity in sewage treatment systems

Table 36: Summary of Microbiological activity in sewage treatment systems

Species	Value	Remarks	Reference
Activated sewage sludge	EC50 (3 h) > 100 mg/l	OECD 209	Registration dossier, (study report 2010).

The microbiological toxicity data given in the registration dossier are summarised in Table 36. L4 is not toxic to activated sewage sludge at concentrations up to 100 mg/l.

The eMSCA notes that no chemical analysis was performed and the test substance was volatile. The Registrant(s) note that the study was performed in excess of the water solubility of L4 (100 mg/l vs. 0.0067 mg/l).

In the registrations for L3 and L5, a read-across table summarising the results of 12 other microorganism tests is also provided as supporting information. None of these were reported to exhibit toxicity.

Overall, the weight of evidence is considered by the eMSCA to be adequate to indicate that there is not a significant concern for micro-organism toxicity up to the limit of solubility for L4.

PNEC STP: 1 mg/L, derived from the EC50 value with an assessment of 100.

7.8.4. Summary of the environmental hazard assessment

The available ecotoxicity data show that L4 does not cause adverse effects in fish, aquatic invertebrates and algae when exposed at concentrations up to the water solubility limit in the test media.

No effects have been seen with L4 up to a concentration of 68 mg/kg dry weight in a study with sediment organisms (*Hyallela azteca*). Furthermore, no effects were observed in the study on *Lumbriculus* up to a maximum (mean measured) concentration of 17 mg/kg dw using natural sediment.

7.8.5. PNEC derivation and other hazard conclusions

Table 37: PNEC derivation

PNEC DERIVATION AND OTHER HAZARD CONCLUSIONS		
Hazard assessment conclusion for the environment compartment	**Hazard conclusion**	**Remarks/Justification**
Freshwater	n/a	The Registrant(s) have not derived any aquatic PNEC because of the lack of effects in the available tests, which include three chronic results.
Marine water		
Intermittent releases to water		
Sediments (freshwater)	Read across from Lumbriculus for L3, with a NOEC of 18.6 mg/kg dwt), the eMSCA derives: $PNEC_{sed}$ = 1.86 mg/kg dwt	Assessment factor: 10
Sediments (marine water)	Using the Lumbriculus NOEC of 18.6 mg/kg dwt, the eMSCA derives: $PNEC_{sed=}$ 0.186 mg/kg dwt	Assessment factor = 100
Sewage treatment plant	PNEC (STP) >1 mg/L	The Registrant(s) derives the PNEC from the EC50 value with an assessment of 100.
Soil	n/a	The Registrant(s) have not derived any PNEC soil because of the lack of effects in the available tests, which include one acute and one chronic result.
Air	No value	The Registrant(s) have not derived a PNEC air. This is justified by the lack of indication of abiotic effects in the atmosphere.
Secondary poisoning	PNEC oral: 0.83 mg/kg food	Assessment factor: 300 Based on a NOAEL (adverse liver weight increase) of 25 mg/kg bw/d in the 28-d oral repeat dose study[20].

7.8.6. Conclusions for classification and labelling

There are no effects in the acute or chronic aquatic toxicity tests. Therefore, the eMSCA considers that the substance needs not to be classified for the environment.

[20] Conversion factor NOAEL to NOEC = 10; assessment factor = 300.

7.9. Human Health hazard assessment

No specific concerns for human health were listed on the CoRAP. The human health hazard assessment was focused on the end-points of relevance to the 'T' criterion, as given in the criteria for the identification of PBT substances in REACH Annex XIII; as such, only the end-points carcinogenicity, germ cell mutagenicity, Unless otherwise stated, the eMSCA has consulted the original study reports and where this has been done the reliability scores assigned are those of the eMSCA and not the Registrant(s). A literature review conducted by the eMSCA did not identify any further information (see Section 7.14). Where the registration dossier includes data from other members of the analogue group to inform on L4 a summary of the data and the conclusions from the relevant evaluation document, along with the Registrant(s) justification for read-across are presented. This approach has similarly been applied where the eMSCA has used data from other members of the analogue group to inform on the substance under consideration.

7.9.1. Toxicokinetics

Not relevant to the targeted evaluation.

7.9.2. Acute toxicity and Corrosion / Irritation

Not relevant to the targeted evaluation.

7.9.3. Sensitisation

Not relevant to the targeted evaluation.

7.9.4. Repeated dose toxicity

7.9.4.1. Repeat-dose toxicity: oral

The repeated-dose oral toxicity of decamethyltetrasiloxane (L4) has been investigated via the oral route in rats and rabbits. In rats, these studies were a non-guideline range-finding study and a guideline 28-day oral study (OECD 407). The summaries of two longer-duration studies, one in rats and one in rabbits, were included in the dossier. However, because they lacked key information they did not contribute to an understanding of the repeated-dose toxicity of L4.

Table 38: Summary of repeated-dose studies via the oral route

Method	Results	Remarks
7 day range-finding study (oral, gavage) Rat (Sprague-Dawley) 100, 300, 1000 mg/kg/day Vehicle: corn oil (dried & deacidified) *5/sex/dose* Non-guideline Registration dossier 7.5.341 (2009)	**At 100 mg/kg bw/day** ↑mean liver-to-body weight ratio. Enlargement of the liver (1/5 males and 1/5 females). Reddish foci on the thymus (1 female) and reddish thymic discolouration (1 male). Enlargement and dark red discolouration of the mediastinal lymph nodes (1 female). **At 300 mg/kg bw/day,** ↑ mean absolute liver weight and the mean liver-to-body weight ratio. Enlargement liver (4/5 males and 3/5 females). **At 1000 mg/kg bw/day (above the level for classification)** Statistically significantly ↑mean absolute liver weight and mean liver-to-body weight ratio (both sexes). Enlargement of liver (4/5 males and 4/5 females). Reddish foci on the thymus (2 females). The mean absolute and relative thymus weights significantly ↑ (males). NOAEL: none set as this was a range-finding study.	Test material: Decamethyl-tetrasiloxane (L4) Reliability: 4 Reliability proposal from Registrant(s). Original study report not consulted by eMSCA.

Method	Results	Remarks
28 day repeat dose study (oral, gavage) Rat (Sprague-Dawley) 25, 250 and 1000 mg/kg/day Vehicle: corn oil *5/sex/dose + 5/sex/dose recovery groups (control and high dose only)*- OECD TG 407 Guideline value for classification for STOT-RE Cat 1 ≤30 mg/kg bw/d and Cat 2 ≤300 mg/kg bw/d Registration dossier 7.5.406 (2010)	**Control** Histopathology: Perilobular fatty liver (3/5 females; mean severity 1.0*) **25 mg/kg bw/d** Haematology: significant reductions in the mean relative basophil and the mean absolute monocyte counts in males and females, respectively Clinical chemistry: Significantly ↑ blood glucose levels and ↓total bilirubin levels (both sexes). Significantly ↓ aspartate aminotransferase activity (females) and significant ↓ creatine kinase Histopathology: ↑ Incidence and severity of perilobular fatty change in the liver (5/5 females; mean severity 1.2*) **250 mg/kg bw/d** Organ weights: Significantly ↑ absolute liver weights (32.3% and 32.8%, males and females respectively), mean liver-to-body weight ratios and mean liver-to-brain weight ratios (both sexes). Gross pathology: accentuated lobular pattern on the liver (both sexes). Clinical chemistry: Significantly ↑ blood glucose (males) and significantly ↓ total bilirubin (both sexes). Significantly ↓ aspartate aminotransferase (both sexes) and significantly ↓ alkaline phosphatase activity (females), significantly ↓ albumin values (both sexes) Histopathology: protoporphyrin accumulation (minimal to slight) in the intrahepatic bile duct (1/5 males). ↑ severity of perilobular fatty liver (5/5 females; mean severity 1.8*) (severity not statistically significant) **At 1000 mg/kg bw/d (above the level for classification)** Organ weights: At the end of treatment significantly ↑ absolute liver weights (23.3% and 60.7% males and females, respectively), mean liver-to-body weight ratios and mean liver-to-brain weight (both sexes). Changes not fully reversible in females. Clinical chemistry: ↑ blood glucose, ↓ total bilirubin, ↓ lactate dehydrogenase activity, ↓ phosphorus, ↓ albumin and ↓ albumin/globulin ratio (both sexes). In males ↑ urea, ↑ potassium and chloride and in females, ↑ cholesterol, ↓ aspartate aminotransferase, ↓ alkaline phosphatase activity, ↓ creatine kinase, ↑ phospholipid levels, ↑ gamma glutamyltransferase, ↑ sodium and changes in total proteins (females). After the recovery period: ↓ total bilirubin, ↓ mean aspartate aminotransferase, and calcium (females). After recovery, ↑ absolute and relative thyroid weights (not apparent at end of treatment (males)), ↑ mean kidney-to-brain weight ratio (females). Gross pathology: accentuated lobular pattern on the liver (both sexes). Histopathology: protoporphyrin accumulation in the intrahepatic bile duct (minimal to slight in 1/5 males) and thyroid follicular cell hypertrophy (minimal severity in 1/5 males). ↑ Incidence and severity of perilobular fatty liver (5/5 females; mean severity 2.8* and 1/10 males, mean severity 1.0*). With the exception of	Test material: decamethyl-tetrasiloxane (L4) Reliability:1

Method	Results	Remarks
	hepatocellualar hypertrophy these changes were still present at the end of the recovery period. Immunohistochemisty: α-2u-globulin accumulation (males) Locomotor activity: Slight ↑ values in early stages of the locomotor activity (both sexes) and ↑ mean locomotor activity from 10-20 minutes, 20-30 minutes and from 0-60 minutes (males). NOAEL: 25 mg/kg bw/d based on liver weight increases of >30% in both sexes. This was accompanied by bile duct proliferation and protoporphyrin accumulation at 250 mg/kg bw/d which showed progression at higher dose levels in males and changes in clinical chemistry indicative of liver effects in females. **Severity grades for clinical symptoms assigned as follows: 0=not present, 1 = present/slight, 2= moderate, 3=marked.*	
12 month feeding study (oral, feed) Rat Dose: Not clear *5/sex/dose* Non-guideline Registration dossier 7.5.055 (1966)	No adverse effects reported.	Test material: Me3EB 200 Fluid, 1.5CS (Siloxane). Name not specified; no further information available. Reliability: 4 Reliability proposal is the Registrant(s) Original study report not consulted.
8 month feeding study (oral, feed) Rabbit (Albino) Dose: Not clear *3/sex/dose* Non-guideline Registration dossier 7.5.054 (1965)	No adverse effects reported.	Test material: Me3EB 200 Fluid, 1.5CS (Siloxane). Name not specified; no further information available. Reliability: 4 Reliability proposal from Registrant (s). Original study report not consulted.

In a non-guideline range-finding study, rats were dosed with decamethyltetrasiloxane (L4) over a period of 7 days. No deaths occurred at any of the doses tested. The main target organ was the liver. Increases in mean absolute liver weight were observed in both sexes at all dose levels, as was enlargement of the liver. The other notable findings were reddish foci on the thymus, reddish thymic discolouration and discolouration of the mediastinal lymph nodes, but these occurred at low incidence and no dose response was observed.

In a guideline 28-day oral study according to OECD 407, rats were dosed with L4 for 28-days. No deaths occurred at any of the doses tested. At doses below the guidance value for classification for STOT-RE Category 2 (≤300 mg/kg bw/d) the main effect was on the liver. Liver weight increased by >30% in both males and females at doses of 250 mg/kg bw/d. Other findings associated with the liver included an accentuated lobular pattern on the liver (both sexes) and protoporphyrin accumulation in the intrahepatic bile duct and bile duct proliferation (males) at 250 mg/kg bw/d and above. Perilobular fatty change was also observed in females, although these changes were not statistically significantly different from the controls. The incidence increased from 3/5 animals in the control groups compared to 5/5 in all treatment groups, while the mean severity score showed a dose-related increase but remained in the present/slight category at doses up to and including 250 mg/kg bw/d. At this dose, changes in levels in clinical chemistry are minimal and are not considered biologically relevant. Changes in haematology were of low magnitude and are similarly not biologically relevant. At the top dose, changes in clinical chemistry were consistent with liver toxicity, however this is above the guidance value for classification.

NOAEL of 25 mg/kg bw/d in males based on liver weight increases of >30% and bile duct proliferation and protoporphyrin accumulation at 250 mg/kg bw/d which showed progression at higher dose levels. The eMSCA also proposes a NOAEL in females of 25 mg/kg bw/d, based on increases in liver weights of >30% and changes in clinical chemistry indicative of liver effects at 250 mg/kg bw/d.

Two chronic studies in rats and rabbits performed with methylsiloxanes were also submitted in the dossier, but in the absence of methodological details and dose levels these are not informative.

7.9.4.2. Repeat-dose toxicity: inhalation

Two repeated-dose studies were carried out via the inhalation route; a combined repeat dose study with a reproduction/developmental screening (OECD 422) and a 90-day repeat dose study according to OECD 413. The results from the combined study that are relevant to reproductive toxicity are described in Section 7.9.7

Table 39: Summary of repeated-dose studies via the inhalation route

Method	Results	Remarks
90 day Repeat dose study + 28 day recovery (inhalation 6 hours daily whole body) Rat (Sprague-Dawley) 0, 70 or 400 ppm (nominal) (vapour) equivalent to 0, 0.9 and 5.1 mg/l/6h/d or a calculated internal dose* of 0, 243 and 1377 mg/kg bw/d *10/sex/dose + 10/sex/dose recovery groups (control and high dose only)* OECD TG 413 Guideline value for classification for STOT-RE Cat 1 ≤0.2 mg/l/6h/d and Cat 2 ≤1 mg/l/6h/d Registration dossier 7.5.464 (2010)	**0 ppm (Control)** Two animals died (cause unknown). Two neoplasms (not specified) were reported in males. Alveolar macrophages (1/10 males; minimal severity). **At 70 ppm (equivalent to approx. 0.9 mg/l or an internal dose of 240 mg/kg bw/d)** No biologically significant and/or treatment related findings. **At 400 ppm (equivalent to approx. 5.1 mg/l or an internal dose of 1377 mg/kg bw/d) (above the concentration for classification)** Transient changes in food consumption and body weight gain (both sexes, recovery group). Organ weight: ↑ liver weight to body weight ratio (8% main females group). Urinalysis: ↓ urine volume, and ↑ urobilinogen (males main group; not seen in recovery group). Statistically significant difference also reported in urobilinogen (recovery group females).	Test material: decamethyl-tetrasiloxane (L4) Reliability: 1

Method	Results	Remarks
	Microscopic : ↑ incidence of alveolar macrophages (2/10 males and 5/10 females; minimal severity) (statistical significant in females) Neoplasms: benign subcutaneous fibroma (common skin lesion) (1 male) NOAEC: >400 ppm (equivalent to 5.1 mg/l/6h/d or an inernal dose of 1377 mg/kg bw/d).	
Combined repeated dose and reproduction/ developmental screening (inhalation, vapour, whole body) Rat (Sprague-Dawley) male/female 0 and 400 ppm (equivalent to ~5.1 mg/l/day) for 6 hours/day or a calculated internal dose* of 0 and 1377 mg/kg bw/d 10 per sex/group for -28/29 days (males/females) (toxicity group) -15 days pre-mating, during the mating period up to and including day 19 of gestation (reproductive group females) OECD TG 422 Guideline value for classification for STOT-RE Cat 1 ≤0.6 mg/l/6h/d and Cat 2 ≤3 mg/l/6h/d Registration dossier 7.5.346 (2007)	The tested concentration was above the cut-off value for classification No deaths and no significant treatment-related clincal signs of toxicity. Effects seen in the toxicity phase animals: Significant ↑ body weight gains in 3rd week of gestation. ↓ Food consumption (Weeks 1 and 2) (within historical control data) and ↓ total food consumption (males). No differences in absolute organ weights. Spleen to body weight ratio slightly ↓ (toxicity group females). No histopathological correlate, nor any effect of exposure in other lymphoid tissues. This was considered to be random variation and not of toxicological significance. No gross lesions attributed to the test substance. No functional or neurological effects. NOAEC: 400 ppm (equivalent to 5.1 mg/l/6h/d or an internal dose of 1377 mg/kg bw/d) for the systemic toxicity. Fertility and offspring effects reported at Section 7.9.7.	Test material: decamethyltetrasiloxane (L4) Reliability: 1

* Calculated as follows: $NOAEL_{internal}$ (mg/kg bw/d) = $NOAEC_{inhalation}$ (mg/l) x 45 l/kg bw/h (rat respiration rate) x 6 (daily inhalation exposure) x 1 (default respiratory absorption of 100%).

In a 90-day inhalation study conducted in accordance with OECD TG 413, decamethyltetrasiloxane (L4) was well tolerated at concentrations of 70 and 400 ppm. There were no clinical signs or treatment-related effects associated with exposure on body weights, food consumption, ophthalmology or neurobehaviour. Significant changes in clinical chemistry, haematology and urinalysis may be treatment-related, however they are not considered to be biologically significant as they show no dose response and fall within the reported range of historical control data. Similarly, changes in organ weight are not considered toxicologically significant as there were no effects observed in the underlying histopathology. The only treatment-related microscopic finding was an increase in the incidence of alveolar macrophages in the highest concentration group which reached statistical significance in females. This was also observed but to a lesser extent in the control group. This is a common finding in inhalation studies and, in the absence of other findings in the lung, is not considered toxicologically significant. Based on the results of this study a NOAEC for L4 for systemic toxicity in male and female rats is considered to be >400 ppm (5.1 mg/l/6h/d).

In a combined repeat dose inhalation study, with reproductive/developmental screening carried out largely according to OECD TG 422, no clinical signs or effects on body weight and food consumption were reported at the only tested concentration of 400 ppm (5.1 mg/l/6h/d). The study deviated from the OECD test guideline in that only a single dose was tested. However, as this exceeded the guidance values for classification for STOT-RE, it is considered reliable for concluding on STOT classification. There were no treatment related changes on neurobehaviour, haematology, clinical chemistry, organ weights or histopathology. Based on these results, a NOAEC of 400 ppm (5.1 mg/l) is proposed for the systemic toxicity of L4. Effects on reproductive endpoints are considered under section 7.9.7.

7.9.4.3. Summary of repeated-dose toxicity

The repeated-dose toxicity of L4 was investigated via the oral and inhalation routes in rats and rabbits. The main findings following oral dosing were on the liver.

Increased liver weight was reported in both males and females at doses below the guidance value for classification in the 7-and 28-day oral studies. In the 28-day study it exceeded 30% (the magnitude of change is not reported in IUCLID for the 7-day range-finding study). This was accompanied by an accentuated lobular pattern on the liver in both sexes, protoporphyrin accumulation (minimal to slight) in the intrahepatic bile duct and a non-statistically significant increase in the incidence and severity of perilobular fatty change (minimal to slight). In the studies via the inhalation route, effects on the liver were confined to doses above the guidance value for classification. Effects on the liver were considered to be adaptive. Changes in clinical biochemistry were consistent with an effect on the liver, although these are not considered toxicologically significant.

A classification for STOT-RE is indicated when toxic effects that may include the following descriptions occur at or below 300 mg/kg bw/d in a 28-day oral rat study or 1mg/l in a 90 day inhalation (vapour) rat study.

a) Morbidity or death resulting from repeated or long-term exposure
There were no treatment-related deaths or cases of moribund animals at any concentration.

b) Significant functional changes in the central or peripheral nervous systems or other organ systems
There were no such changes in any organ systems.

c) Any consistent and significant adverse change in clinical biochemistry, haematology or urinalysis parameters
There were no such changes at doses below the guidance values.

d) Significant organ damage noted at necropsy and/or subsequently seen or confirmed at microscopic examination
There were no such effects at doses below the guidance values.

e) Multi-focal or diffuse necrosis, fibrosis or granuloma formation in vital organs with regenerative capacity
There were no such effects.

f) Morphological changes that are potentially reversible but provide clear evidence of marked organ dysfunction (e.g. severe fatty change in the liver)
In the 28-day repeated-dose oral study, perilobular fatty liver change that increased in incidence and severity with dose was recorded in treated females at dose levels below the guidance value for classification. This finding was not statistically significantly different from the occurrence and severity seen in control animals. Furthermore, while the mean score for severity did increase, these scores were all within the level assigned as present/slight. While not completely reversible (in the top dose group which was above the level for classification), these findings were observed at lower incidence and

severity in the recovery group. This incidence of perilobular fatty liver was not accompanied by findings such as degeneration or inflammation. Perilobular fatty liver change was not seen in males at doses below the guidance value for classification. Overall, the finding of perilobular fatty liver is not considered adverse.

Protoporphyrin accumulation was recorded at minimal to slight severity in one male at doses of 250 mg/kg bw/d. This is below the guideline value for classification. At this incidence and severity, the finding is not statistically significantly different from the control group and is not considered adverse.

No other morphological findings were reported in the liver at doses below the guideline for classification in animals dosed via the oral route, nor were any effects reported at levels below the guideline levels for classification in either of the studies in which animals were exposed by the inhalation route.

g) Evidence of appreciable cell death (including cell degeneration and reduced cell number) in vital organs incapable of regeneration
There were no such effects.

Additionally, there were no generalised changes that involved several organ systems or significant/severe changes in the general health status of the animals.

Overall, based on the data from the repeated-dose toxicity studies, decamethyltetrasiloxane (L4) does not meet the criteria for classification for STOT-RE.

7.9.5. Mutagenicity

7.9.5.1. *In vitro* genotoxicity data

The genotoxicity of L4 was investigated *in vitro* in a bacterial reverse mutation assay and a mammalian cell gene mutation aberration test. The results of the genotoxicity testing are summarised in Table 40.

Table 40: Summary of *in vitro* genotoxicity studies

Method	Results	Remarks
Bacterial reverse mutation Assay *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 *and E. coli WP2 uvrA* (with and without metabolic activation) OECD TG 471 Test concentrations: 50, 150, 500, 1500 and 5000 µg/plate Duplicates of each dose. Appropriate positive controls and solvent controls. Registration dossier 7.6.1.1.317 (2005)	Test reported as negative both in the presence and absence of metabolic activation. No cytotoxicity was reported at concentrations up to the limit dose.	Test Material: Decamethyl-tetrasiloxane (L4) Reliability*: 1
Mammalian cell gene mutation assay Mouse lymphoma L5178Y TK OECD TG 476 Test concentrations: 4 hour exposure (with & without metabolic activation: 0, 12.5, 25, 50, 100, 150 and 200 µg/ml 24 hour exposure (without metabolic activation): 0, 1.56, 3.13, 6.25, 12.5, 18.75, 25, 37.5 and 50 µg/ml Appropriate positive controls and solvent controls. Registration dossier 7.6.1.3.080 (2010)	Test reported as negative both in the presence and absence of metabolic activation. Precipitation observed at doses of ≥100 µg/ml at end of 4-hour exposure period Cytotoxicity observed at doses of 12 – 24 µg/ml following 24-hour exposure.	Decamethyl-tetrasiloxane (L4)

L4 has been tested *in vitro* in bacterial and mammalian cell systems in an Ames test and an *in vitro* mouse lymphoma assay. Both were carried out following the OECD guidelines and according to GLP. The results of both tests are negative in both the presence and absence of metabolic activation.

A further *in vitro* assay carried out on a closely related substance (octamethyltrisiloxane (L3)) is included in the registration dossier (*in vitro* Mammalian Chromosome Aberration Test (2008)). The study was carried out following OECD TG 473 and in accordance with GLP and gave a negative result.

Overall, the *in vitro* data are negative.

7.9.5.2. *In vivo* gentoxicity data

No *in vivo* genotoxicity data were submitted in the registration dossier. However, L4 was negative *in vitro* and therefore the trigger for *in vivo* testing is not met.

7.9.5.3. Human information

No information available.

7.9.5.4. Summary and discussion of mutagenicity

Two *in vitro* studies performed with L4 were submitted as part of the registration dossier; one study was conducted in bacterial cells and a second in mammalian cells (L5178 Y TK mouse lymphoma cells). The registration dossier also included a chromosome aberration test performed in Chinese Hamster Ovary cells with the closely related structural analogue L3. All three studies reported negative results.

The Registrant(s) have proposed that data from a chromosome aberration test with the structural analogue L3 can be used to inform on the genotoxicity of L4. The proposal to read-across is based on the finding that L4 and L3 both hydrolyse slowly, to produce dimethylsilanediol and trimethylsilanol. It is stated by the Registrant (s) that neither siloxanes nor silanediols/silanetriols are likely to contribute to genetic toxicity.

Further similarities that are considered are that both L4 and L3 have long hydrocarbon side-chains and that neither substance contains any functional groups that are associated with genetic toxicity. Furthermore, L3 is more water soluble than L4 and therefore theoretically will have a higher bioavailability.

No *in vivo* testing was reported in the registration dossier.

Overall, based on the available information, L4 is not considered to be mutagenic.

7.9.6. Carcinogenicity

No chronic repeated-dose study was submitted in the registration dossier to enable the assessment of the carcinogenic potential of the registered substance. However, the genotoxicity profile has been shown to be negative *in vitro*.

7.9.7. Toxicity to reproduction (effects on fertility and developmental toxicity)

Information on reproduction and development is available from a combined repeat dose toxicity study with reproduction/developmental screening (OECD 422) and a developmental toxicity test (OECD 414). Results for the reproductive group of the combined study are reported in Table 41 below. Results from the toxicity group are reported under Section 7.9.4.2.

Table 41: Summary of reproductive effects from the combined repeated-dose study with reproductive/developmental screening and prenatal developmental toxicity study

<table>
<tr><th>Method</th><th>Results</th><th>Remarks</th></tr>
<tr><td>Combined repeated dose and reproduction/ developmental screening (inhalation, whole body)
Rat (Sprague-Dawley) male/female
10 per sex/group
0 and 400 ppm (equivalent to approximately 5.1 mg/l) for 6 hours/day or a calculated internal dose* of 0 and 1377 mg/kg bw/d
Equivalent or similar to OECD TG 422
Registration dossier 7.8.2.042 (2007)</td><td>Parental
See Section 7.9.4.2

Fertility
No effect on testes or epididymides weights or histopathology. No other parameters examined.

Three dams in the treated group failed to deliver a litter. One of these showed signs of parturition (blood discharge) on day 25 but no pups were found although 7 implantation sites were present. There were no implantation sites present in the other two animals. All control animals produced litters.

In dams that successfully produced litters, there were no changes in litter size, male-to-female ratio, pup body weights or the pup survival. There were no effects on duration of gestation, number of implantation sites, number of corporea lutea, mating and fertility indices, litter size and weight or ratio live births/litter.

Developmental (Offspring)
No adverse effects on pups up to day 4 post partum. Effects on histopathology and organ weight in pups not investigated.

NOAEC: 400 ppm (equivalent to approximately 5.1 mg/l/ 6 hours/day or a calculated internal dose of 1377 mg/kg bw/d for both fertility and offspring.</td><td>Test material: decamethyl-tetrasiloxane (L4)
Reliability 1</td></tr>
<tr><td>Developmental toxicity study

According to OECD TG 414 (Prenatal Developmental Toxicity Study) and EPA OPPTS 870.3700

Rat (Crj: CD(SD)) time-mated females, 24 per dose

oral: gavage: 0, 100, 300 and 1000 mg/kg bw/day

Vehicle: corn oil – (dried and deacidified corn oil)

Exposure: GD 6-20 (Daily)

[2020]</td><td>Maternal toxicity

There were no clinical signs considered related to treatment and there was no adverse effect of treatment on body weight gain or food intake during gestation at 100, 300 or 1000 mg/kg bw/day.
There were, however, effects seen on the thyroid glands. Particularly an increase in the incidence of diffuse follicular cell hypertrophy, when compared to controls, was seen in females given 300 or 1000 mg/kg bw/day.
Serum TSH concentrations on Day 20 of gestation were higher in all treated groups. As we did not have access to the full study report we do not know how much higher the levels were, but according to the information on the dissemination site the levels were only slightly higher and there was no dose-response.
There was a slight decrease in the mean serum thyroxine (T4) and triiodothyronine (T3) concentration in all treated groups, although there was no dose-response, according to the information on the dissemination site.
There was also an increase in liver weights seen in all treated females. A connection between liver toxicity and an increase in thyroid stimulating hormone (TSH) levels is known to happen. A subsequent reduction in levels of T4 and T3 was seen, as would be expected in a normal physiologically functioning system.
There was however a higher incidence of follicular cell hypertrophy in the two highest dose levels which was dose related.

Hypertrophy, follicular cells in the thyroid gland for females on Day 20 after mating:
<table>
<tr><th>Dose (mg/kg bw/day)</th><td>0</td><td>100</td><td>300</td><td>1000</td></tr>
<tr><td>Minimal</td><td>2</td><td>3</td><td>8</td><td>13</td></tr>
<tr><td>Total</td><td>2</td><td>3</td><td>8</td><td>13</td></tr>
</table>
</td><td>Test material: decamethyl-tetrasiloxane (L4)
Reliability 1
(the eMSCA did not have access to the full study report)</td></tr>
</table>

Method	Results	Remarks
	<table><tr><td>Number of tissues examined</td><td>20</td><td>20</td><td>19</td><td>20</td></tr></table> Maternal reproductive toxicity: no effects observed NOAEL: 100 mg/kg bw/day based on a higher incidence of follicular cell hypertrophy in the two highest dose levels. **Fetuses:** Litter and foetal weights were unaffected by maternal treatment with decamethyltetrasiloxane at 100, 300 and 1000 mg/kg bw/day. There was no effect on embryo-foetal survival, live litter size or sex ratio at 100, 300 or 1000 mg/kg bw/day. No major abnormalities that were considered treatment-related were seen at foetal examination. There were however some minor abnormalities, variations, including an increase in incidence of delayed ossification across all treated groups and lens shape variation at 1000 mg/kg bw/day. The incidences of these variations were not given. Probably these effects are too mild to warrant a classification, however it is not quite clear whether this can be considered non-adverse. There was no indication of embryo/fetal toxicity or teratogenicity at any dose level tested. NOAEL: 300 mg/kg bw/day, based on increased incidence of variations in the highest dose group. Overall developmental toxicity: no	

* Calculated as follows: $NOAEL_{internal}$ (mg/kg bw/d) = $NOAEC_{inhalation}$ (mg/l) x 45 l/kg bw/h (rat respiration rate) x 6 (daily inhalation exposure) x 1 (default respiratory absorption of 100%).

7.9.7.1. Effects on fertility

In the combined repeated dose and reproduction/ developmental screening study three female rats, where there was evidence of copulation, failed to deliver a litter. One of these animals showed signs of parturition on day 25 and although no pups were found seven implant sites were present. There were no implantation sites recorded in the other two animals.
There were no treatment-related effects on weight or histopathology of the male reproductive organs.
There were no effects on the mean number of corporea lutea or mean mating and fertility indices. In dams that successfully produced litters, the duration of gestation, mean number of implantation sites, mean litter size and weight and mean ratio of live births/litter were unaffected by treatment.
A NOAEC of 400 ppm for fertility has been identified; however, as a specific reproductive effect cannot be ruled out, the eMSCA considers that it is not possible to set a NOAEC for fertility based on the results of this study when it is considered in isolation. These results also raise a concern over the potential of L4 to affect reproduction (fertility)/parturition. However, two reproductive toxicity studies have been carried out using the closely related substance hexamethyldisiloxane (L2) and data from these can be used to inform on L4 and support a NOAEC of 400 ppm. In the L2 studies, animals were exposed to L2 at concentrations approximately six times that used in the L4 screening study included in the current dossier.
In the developmental toxicity study there were no effects seen on reproductive parameters. One female in the middle dose group did not become pregnant, but apart from that the

only effects seen in the dams were increased liver weights, increased TSH and lower T3 and T4 and a dose-response increase in minimal hypertrophy in the follicular cells of the thyroid glands. The NOAEL was set at 100 mg/kg bw/day based on the hypertrophy of the thyroid glands. The NOAEL for reproductive parameters was the highest dose levels.

In a two generation study Sprague Dawley rats were exposed to L2 at doses of up to 5000 ppm. No treatment-related effects were observed on sexual function or fertility at any of the concentrations tested. The mean number of pups born, live litter size and the percentage of males per litter at birth were unaffected by exposure at all concentration levels tested. A NOAEC for L2 of 5000 ppm (33 mg/l) for sexual function and fertility effects was identified.

A one generation study is also available in which Sprague Dawley rats were treated with L2 up to doses of 5000 ppm. No histopathological findings were observed in the tissues examined (cervix, coagulating gland, epididymis, ovaries, mammary gland, pituitary gland, prostate, seminal vesicles, testes, thyroid, uterus, vagina, vas deferens) nor were there any treatment-related effects noted on reproductive parameters (days between pairing , mating indices, fertility indices and duration of gestation), parturition or litter size. A NOAEC for L2 of 5000 ppm for fertility was identified from this study.

The eMSCA considers that data from full generational studies with L2 can be used to support the conclusion that the findings on fertility/parturition reported in the reproductive screening study with L4 are not adverse. This is justified based on the physicochemical, toxicokinetic and toxicological properties of each of the substances. Both L2 and L4 are members of an analogue group of linear and cyclic siloxanes containing no reactive functional groups. A characteristic of the group is that all the substances have high log Kow (increasing with increasing chain length) and low water solubility (decreasing with increasing chain length). L2 is the smallest of the linear siloxanes with the lowest molecular weight, shortest chain length and highest solubility in water. It can therefore be concluded that it will have a higher bioavailability than L4. As such, L2 can be considered to represent a worst case scenario. No data is available on the metabolism of L4.

However the Registrant(s) have stated that L4 hydrolyses to dimethylsilanediol and trimethylsilanol, both of which are reported as metabolites in the toxicokinetic study with L2. L2 also shows similar effects to L4 following repeat dosing via the oral and inhalation routes, with the liver and kidney in rats being the target organs.

Consequently, while there were some effects observed following treatment with L4, there were no effects on reproductive parameters in the developmental toxicity study and data from L2 does not support the view that these are the result of an effect on fertility and therefore a NOAEC for L4 of 400 ppm (5.1 mg/l/6h/d) is identified for fertility based on the combined screening study.

7.9.7.2. Effects on offspring

In the combined repeated dose and reproduction/ developmental screening study no adverse effects were reported for pups up to day 4 post partum. Investigation of effects on histopathology and organ weights in pups was not conducted. Based on the results of this study a NOAEC for L4 for developmental (offspring) toxicity in male and female rats is 400 ppm (approximately 5.1 mg/l/6h/d).

In the developmental toxicity study there were no effects on litter and foetal weights, nor on embryo-foetal survival. There was a certain increase in some variations; delayed ossification across all treated groups and lens shape variation at 1000 mg/kg bw/day. The incidences of these variations were not given and as we did not have access to the full study report it is difficult to determine whether this is non-adverse. Probably these effects are too mild to warrant a classification.

There was no indication of embryo/fetal toxicity or teratogenicity at any dose level tested.

NOAEL: 300 mg/kg bw/day, based on increased incidence of variations in the highest dose group

7.9.7.3. Summary of reproductive toxicity

Effects on Sexual Function and Fertility

There was one repeated-dose study with combined reproductive/developmental screening and one developmental toxicity study on L4. In the combined study, in males, no histopathological effects were observed on testes or epididymis. In dams that successfully produced litters, there were no significant changes in any relevant parameters. Three dams failed to produce litters, and based on the information in the study it is not possible to determine whether this was a specific reproductive effect. However, studies carried out with L2 found no effects on fertility or sexual function. Therefore, on a weight of evidence basis it is concluded that L4 does not have an effect on sexual function, fertility or parturition and no classification is proposed for this endpoint. The NOAEC for fertility is 400 ppm (5.1 mg/l).

In the developmental toxicity study all but one female in the middle dose became pregnant and no reproductive parameters were affected. A NOAEL of 1000 mg/kg bw/day was set for reproductive parameters, however a NOAEL of 100 mg/kg bw/day for maternal toxicity was set based on increased hypertrophy of follicular cells in the thyroid glands.

Developmental effects

In the combined study no adverse effects on pups up to day 4 post partum were observed. Based on the results of this study a NOAEC of 400 ppm (equivalent to 5.1 mg/l) was derived. In the developmental toxicity study no effects were seen apart an increase in some variations in the highest dose group. A NOAEL of 300 mg/kg bw/day was set based on the increase in variations at 1000 mg/kg bw/day. No classification is proposed for this endpoint.

7.9.8. Hazard assessment of physico-chemical properties

Not assessed.

7.9.9. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

Not assessed.

7.9.10. Conclusions of the human health hazard assessment and related classification and labelling

The human health hazard assessment was focussed on the end-points of relevance to the 'T' criterion, as given in the criteria for the identification of PBT substances in REACH Annex XIII; as such, only the end-points carcinogenicity, germ cell mutagenicity, reproductive toxicity and repeated-dose toxicity were evaluated. The available data for the remaining end-points (acute toxicity, irritancy, corrosivity, sensitisation) was not evaluated.

There is no information available on the effects of repeated exposure to L4 in humans. Information is available from studies carried out in rats from a 28-day repeated-dose oral study (OECD 407), a 90-day repeated-dose inhalation study (OECD 413) and a repeated-dose toxicity with reproduction/developmental screening (OECD 422). Results from a 7 day range-finding study were consistent with those from the longer-term studies. The consistent findings show an effect on the liver and kidneys. The latter is not relevant to human risk assessment and the liver findings do not meet the criteria for classification. The data therefore do not raise any concerns for specific organ toxicity following repeated exposure to L4.

The mutagenic potential of L4 has been investigated *in vitro* in bacterial and mammalian cell gene mutation assays in which it tested negative. The effect of L4 on chromosome

aberration has not been directly investigated, but the registration dossier includes data on the closely related substance L3, which was found to be negative when tested. The available data do not raise any concerns for the mutagenic potential of L4.

There is no information on the carcinogenic potential of L4, however the results from the *in vitro* genotoxicity testing were negative. Therefore, no specific concerns for carcinogenicity are raised.

The reproductive toxicity of L4 has been investigated in animals in a combined repeated-dose toxicity study with reproductive/developmental toxicity screen (OECD 422). Effects of parturition/fertility raised concerns for this endpoint following exposure to L4. However, the eMSCA considers that data from generational studies with L2 can be used in a weight of evidence approach to conclude on the reproductive toxicity of L4. In animals exposed to much higher concentrations of L2, there were no reproductive effects and this negative finding supports the conclusion that the findings from the L4 screening study are not treatment-related. There were no effects reported on developmental parameters. In addition, no significant effects were reported on the reproductive organs in both the 28-day oral and the 90-day inhalation studies. The data do not raise any specific concerns for fertility, parturition or developmental toxicity.

Overall the data raise no concerns for carcinogenicity, mutagenicity, reproductive toxicity or toxicity following repeated exposure (STOT RE).

Table 42: NOAELs from repeat dose toxicity studies

Study		NOAEL / NOAEC	LOAEL / LOAEC	Effects at the LOAEL
Rat, 28 day oral		25 mg/kg bw/d (males)	250 mg/kg bw/d (males)	Protoporphyrin accumulation in males and increased liver weight together with changes in liver markers and histopathology in females.
Rat, 90 day inhalation		400 ppm (equivalent to 5.1 mg/l	-	accumulation of protoporphyrin pigment. periportal chronic inflammation and bile duct proliferation
Rat, developmental toxicity study	Systemic	100 mg/kg bw/day		Increased minimal hypertrophy of follicular cells of the thyroid gland
	Maternal	1000 mg/kg bw/day		No treatment related effects at highest dose tested
	Fertility	1000 mg/kg bw/day		No treatment related effects at highest dose tested
	Developmental	300 mg/kg bw/day		Some increase in variations at highest dose levels
Rat, combined toxicity with reproductive/ developmental screening	Systemic	400 ppm (equivalent to 5.1 mg/l)	-	No treatment related effects at highest dose tested
	Maternal	400 ppm (equivalent to 5.1 mg/l)	-	No treatment related effects at highest dose tested
	Fertility	400 ppm (equivalent to 5.1 mg/l)	-	No treatment related effects at highest dose tested
	Developmental	400 ppm (equivalent to 5.1 mg/l)	-	No treatment related effects at highest dose tested

7.10. Assessment of endocrine disrupting (ED) properties

Not assessed.

7.11. PBT and vPvB assessment

7.11.1. Assessment of PBT/vPvB properties – Comparison with the criteria of Annex XIII

Persistence

Experimental data for L4 show a hydrolysis half-life of 30.3 days at pH 7 and 25 °C, but the half-life is dependent on temperature and pH. By recalculating hydrolysis half-life to an environmentally relevant temperature of 12 °C and pH 7, a hydrolysis half-life of 130 days can be obtained.
No screening tests are available for the evaluation of ready biodegradability of L4, but read-across to a screening test on ready biodegradability for L3 (0 % in 28 days, OECD 310) has been used, indicating that L4 is not readily biodegradable. Therefore, L4 is considered to meet the screening criteria for P and vP of REACH Annex XIII.

No experimental data on the potential for degradation of L4 in sediments are available. A long sediment degradation half-life of 3.5 – 6.9 years at 12° C has been demonstrated for L3 in a sediment simulation test (OECD 308). The simulation study on L2 (OECD 308) indicates a half-life in sediment of 360 days. These test results can be read across to L4, which is expected to be even more persistent than L2 and L3.

Overall, the available experimental data for L4 and read across from sediment simulation studies for L2 and L3 demonstrate that L4 fulfils the P and vP criteria of REACH Annex XIII.

Bioaccumulation

L4 has a log Kow of 8.21 and therefore fulfils the screening criteria for B and vB of REACH Annex XIII. The BCF for the substance in fathead minnow (*Pimephales promelas*) has been determined to be in the range 6,840-7,540l/kg, when normalised to a 5% lipid content. On this basis it can be concluded that L4 meets the criteria for bioaccumulative (B) and very bioaccumulative (vB) of REACH Annex XIII.

The results of a dietary accumulation study using rainbow trout (*Oncorhynchus mykiss*) are also available for L4, where a lipid normalised and growth-corrected BMF for L4 of 3.8 was estimated by the Registrant(s). Depuration of L4 from rainbow trout was slow when growth dilution was taken into account. The results support the findings of the BCF study, although there are some concerns about the validity of the dietary study.

Overall, aquatic BCF values in the range of 6,840-7,540 l/ kg for L4 significantly exceed the criteria for both bioaccumulative (B) and very bioaccumulative (vB) of REACH Annex XIII.

Toxicity

T-criterion based on human health data:

L4 does not fulfil the T-criterion of REACH Annex XIII based on human health end points.

T-criterion based on ecotoxicity data:

The available ecotoxicity data show that L4 does not cause adverse effects in fish, aquatic invertebrates and alga when exposed at concentrations up to the water solubility limit in the test media. Thus, based on the available ecotoxicity data L4 does not fulfil the REACH Annex XIII T-criterion based on ecotoxicity.

7.11.2. Summary and overall conclusions on the PBT, vPvB properties

Based on the available data for L4 and including read-across test results from the linear siloxanes L2, L3 the substance can be identified as a very persistent and very bioaccumulative (vPvB) substances according to Article 57(e) of REACH.

The REACH Annex XIII criterion for T is not currently met.

7.12. Exposure assessment

Decamethyltetrasiloxane was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB
- Wide dispersive use
- Consumer use

7.12.1. Human health

7.12.1.1. Worker

Human health effects by personal care/cosmetic products have not been assessed, since they are outside the scope of REACH. No hazards have been identified for human health, therefore no exposure assessment and risk characterisation regarding workers and consumers are needed.

7.12.1.2. Consumer

Human health effects by personal care/cosmetic products have not been assessed, since they are outside the scope of REACH. No hazards have been identified for human health, therefore no exposure assessment and risk characterisation regarding workers and consumers are needed.

7.12.2. Environment

During the initial substance evaluation, the environmental exposure section was reviewed, and a general information request was identified and addressed in the decision. The Registrant (s) have provided an updated environmental exposure assessment which has been reviewed. No attempt has been made to replicate calculations provided in updates or new registrations submitted after the initial evaluation.

7.12.2.1. Aquatic compartment (incl. sediment)

Professional and consumer use of personal care products

As specified in the decision, the Registrant(s) were requested to update the exposure information by providing further information and justification on the input parameters used for the exposure assessment for ES3: Professional & consumer use of personal care products or alternatively, provide separate scenarios for professional consumer use and household consumer use of personal care products, including clear justification of the environmental emission factors chosen for each.

This request was based on the fact that Registrant(s) had used the approach from the UK Risk Assessment of D5 (Brooke et al., 2009) to determine the releases to air and water for the environmental modelling. Registrant(s) assumed that the use resulted in 90% of the chemical being released to air and 10% released to water. However, there was no supporting justification why the uses of L4 are the same as for D5. Basically, the environmental emissions from all three personal care product scenarios are described by ERC 8a, where default release factors of 100% to water, 100% to air, 0% to soil are assumed.

“Consumer use releases” of D5 have been assessed for the REACH Restriction dossier for D4 and D5 (ECHA, 2016). This suggests that releases are different depending on whether the personal care product is a “wash-off use” or “leave-on” product. The balance of wash-off and leave-on was not provided in the registration dossier of L4, but is needed for an accurate assessment of the consumer/professional use personal care emission scenario.

Further, it was unclear whether the exposure scenario “use of personal care products” adequately addresses environmental emissions from both professional salons and from household uses. The eMSCA considered that the emissions are probably not the same, for example due to the number of emission days and volumes used at salons compared to individual households.

Registrant(s) have included separate exposure scenarios for professional and consumer uses in the updated registration dossier. In addition, the consumer scenario has been split into leave-on and wash-off scenarios, with an estimate of the tonnage split between wash-off and leave on products provided.

Registrant(s)did refine these exposure estimates to air and water providing additional justification based on a study by Montemayor et al (2013) . The Montemayor et al. study has been discussed in the restriction report of D4/D5 (ECHA 2016). It is noted that there is an apparent dosing error, which when corrected gives the average release to water of around 73% (range: 54 – 93%, based on the 95% confidence intervals). Therefore, the D4/D5 restriction dossier uses release estimates of 100% to water for "wash-off use" as a reasonable worst case. The eMSCA considers that a reasonable worst case assumption of 100% to water should also be made in the L4 dossier, as the data from Montemayor et al. (2013) are insufficient to justify a lower emission factor.

7.12.2.2. Terrestrial compartment

Not assessed

7.12.2.3. Atmospheric compartment

Not assessed

7.12.3. Combined exposure assessment

An assessment of cumulative risk from all registrations has not been conducted. The eMSCA concludes that L4 meets the REACH Annex XIII vPvB criteria. Therefore, Registrant(s) should review their exposure scenarios and risk reduction measures in order to minimize emissions and subsequent exposures of humans and the environment throughout the lifecycle of the substance.

7.13. Risk characterisation

7.13.1. Human health

Not evaluated by the eMSCA.

7.13.2. Environment

The eMSCA derived the freshwater sediment PNEC from read across of a Lumbriculus study for L3. Using the freshwater sediment PNEC derived by the eMSCA from L3 (1.86 mg/kg dw), causes the RCR to exceed one (RCR > 1) for some exposure scenarios of L4. This suggests that there are potentially risks from some uses, which need to be minimized to the extent possible. However, the PNEC is based on a NOEC showing no effects and therefore the potential for risk must be considered with caution.

The eMSCA concludes that L4 meets the REACH Annex XIII vPvB criteria, therefore the Registrant(s) should review their exposure scenarios and risk reduction measures to ensure the minimisation of emissions and subsequent exposure of humans and the environment, throughout the lifecycle of the substance.

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9. Abbreviations

%	Percentage
AOP	Adverse outcome pathway
B	Bioaccumulative
BCF	Bioconcentration factor
BMF	Biomagnification factor
CLP	Classification, labelling and packaging (of substances and mixtures)
CTD	Characteristic travel distance
cm	Centimetre
CoRAP	Community Rolling Action Plan
CSA	Chemical Safety Assessment
CSR	Chemical Safety Report
d	Day
D4	Octamethylcyclotetrasiloxane
D5	Decamethylcyclopentasiloxane
D6	Dodecamethylcyclohexasiloxane
DMEL	Derived Minimal Effect Level
DNEL	Derived No Effect Level
DOC	Dissolved Organic Carbon
DSD	Dangerous Substances Directive
ECETOC TRA	European Centre for Ecotoxicology and Toxicology of Chemicals Targeted Risk Assessment
ECHA	European Chemicals Agency
eMSCA	Evaluating Member State
EPA	Environmental Protection Agency
ES	Exposure Scenario
ERC	Environmental release category (ERC)
EU	European Union
EUSES	European Union System for the Evaluation of Substances
g	Gramme
GC	Gas chromatography
GC/FID	Gas chromatography – Flame Ionisation Detection
GC/MS	Gas chromatography – mass spectrometry
GLP	Good laboratory practice
hPa	Hectopascal
ISO	International Organisation for Standardisation
IUCLID	International Uniform Chemical Information Database
IUPAC	International Union of Pure and Applied Chemistry
kg	Kilogram
kJ	Kilojoule
km	Kilometre
kPa	Kilopascal
K_{oa}	Octanol-air partition coefficient
K_{oc}	Organic carbon-water partition coefficient
K_{ow}	Octanol-water partition coefficient
L	Litre
L2	Hexamethyldisiloxane
L3	Octamethyltrisiloxane
L4	Decamethyltetrasiloxane
L5	Dodecamethylpentasiloxane
LEV	Local Exhaust Ventillation
LSC	Liquid scintillation counting
Log	Logarithmic value
LOD	Limit of detection
LOQ	Limit of quantitation
M	Molar
m	Metre(s)
µg	Microgram
mg	Milligram

min	Minute
mL	Millilitre
mol	Mole
MLoQ	Method limit of quantification
MS	Mass spectrometry
MSCA	Member State Competent Authority
m/z	Mass to charge ratio
nm	Nanometre
NOAEL	No observed adverse effect level
NOEC	No-observed effect concentration
NOEL	No observed effect level
OC	Operational condition
OECD	Organisation for Economic Co-operation and Development
p	Statistical probability
P	Persistent
Pa	Pascal
PBT	Persistent, Bioaccumulative and Toxic
PC	Product category
pg	Picogramme
pKa	Acid dissociation constant
PNEC	Predicted no effect concentration
ppb	Parts per billion
PPE	Personal Protective Equipment
ppm	Parts per million
PROC	Process Category
QSAR	Quantitative structure-activity relationship
r^2	Correlation coefficient
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals (EU Regulation No. 1907/2006)
RCR	Risk characterisation ratio
RH	Relative humidity
RMM	Risk Management Measures
RPE	Respiratory protective equipment
RSS	Robust Study Summary
t	Tonne
T	Toxic (hazard classification)
TE	Transfer efficiency
TG	Test Guideline
UK	United Kingdom
UV	Ultraviolet
vB	Very bioaccumulative
vP	Very persistent
vPvB	Very persistent and very bioaccumulative
wt.	Weight

10. Appendix I: trends in PBT properties across linear siloxanes

L4 is part of a group of related linear siloxanes being evaluated under substance evaluation for similar concerns that they could be PBT/vPvB substances. The other substances are hexamethyldisiloxane (L2), decamethyltetrasiloxane (L3) and dodecamethylpentasiloxane (L5).

The table below summarises the expected trends in this group for different PBT endpoints based on the available information for these chemicals and the cyclic siloxanes D4, D5 and D6 (octamethylcyclotetrasiloxane, EC No. 209-136-7, CAS RN 556-67-2; decamethylcyclopentasiloxane, EC No. 208-764-9, CAS RN 541-02-6 and dodecamethylcyclohexasiloxane, EC No. 208-762-8, CAS RN 540-97-6).

Table 43: Trends for PBT endpoints

	L2 EC 203-492-7	L3 EC 203-497-4	L4 205-491-7	L5 205-492-2
Persistence	increasing half-life →			
Bioaccumulation	← peaks at L3 →			
Toxicity (aq)	Significant toxicity	No effects at L3 and higher (decreasing trend)		
Toxicity (sed)	decreasing trend L2 to L5 →			

Persistence (environmental half-life) is expected to increase with increasing chain length. This is the trend observed for the cyclic siloxanes for sediment half-life. The same trend is expected for the linear siloxanes because of a similar increase in hydrophobicity with increasing chain length based on water solubility and organic carbon partitioning data. Further support for the expected trend in the linear substances comes from the increasing hydrolysis half-lives for L2, L3 and L4 respectively, and the observed trend from the non-standard soil degradation studies.

Fish bioaccumulation, based on BCF, for the category appears to peak at L3. L3 has a larger log Kow value than L2, which explains why the BCF value is larger. Above L3, bioaccumulation decreases with increasing log Kow. This is likely to be due to decreasing bioavailability of the category members. Despite the decreasing trend beyond L3, the BCF value for L4 is still sufficiently large for the substance to meet the vB criteria. L5 is B but not vB. A similar trend is seen for the cyclic siloxanes where the bioconcentration factors decrease from D4 to D6.
The trend in ecotoxicity is inverse to the trend in water solubility in the category. L2 is very toxic to aquatic organism (both Daphnia and algae), but is not “T”. Chronic fish toxicity for L2 remains to be characterised. A complete chronic aquatic dataset is available for L3 and L4 and both show no effects. On this basis, beyond L2 the substances become too insoluble to exhibit effects, and so it is anticipated that L5 would similarly show no aquatic effects.

For the benthic compartment, decreasing bioavailability is also expected to result in a decreasing trend in toxicity along the category.