SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Octamethyltrisiloxane (L3)

EC No 203-497-4

CAS RN 107-51-7

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, octamethyltrisiloxane (L3) was originally selected for substance evaluation in order to clarify concerns about:

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

During the evaluation an additional concern related to exposure of the environment 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 2015 where the following tests were required:
1. Pre-natal developmental toxicity study in rats or rabbits, oral route
2. Long-term toxicity testing on plants
3. Long-term toxicity to terrestrial invertebrates
4. Effects on soil microorganisms

Octamethyltrisiloxane (L3) 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), decamethyltetrasiloxane (L4) 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 eMSCAs 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.

A compliance check on D5 is still ongoing in 2021.

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	
Need for follow-up regulatory action at EU level	X
Harmonised Classification and Labelling	
Identification as SVHC	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

No need for follow-up.

However, the eMSCA considers the data on human health, STOT RE, as borderline.

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

L3 is considered to meet the criteria for very persistent and very bioaccumulative (vPvB) substances according to Article 57(e) of REACH.

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 L3 as an SVHC. In addition to leading to a formal recognition of the vPvB properties, Candidate Listing of L3 will also imply other legal obligations.
Suppliers of substances and mixtures containing L3 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 on the Candidate List. The formal recognition of L3 as a vPvB substance with the subsequent obligations for the supply chain is expected to result in emission reductions of L3.

4.1.3. Restriction

L3 is used by consumers and professional workers mainly in washing/cleaning products and cosmetics and personal care products. The wide dispersive use represents a significant potential for environmental releases.

The eMSCA concludes that L3 is considered to meet the criteria for very persistent and very bioaccumulative (vPvB) substances according to Article 57(e) of REACH. Therefore, all emissions and environmental releases of L3 should be reduced as much as possible.

To avoid regrettable substitution, L3 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) and the restriction on D4, D5 and D6 in consumer and professional products (ECHA, 2020).

Since the inclusion of L3 into CoRAP in 2015 an increase in the aggregated tonnage from 100-1000 tpa to 1000-10 000 tpa has been noted, confirming the increased use of L3 as a potential alternative for D4, D5 and D6.

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 L3 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, octamethyltrisiloxane (L3) was originally selected for substance evaluation in order to clarify concerns about:

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

During the evaluation an additional concern related to exposure of the environment 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 corresponding outcomes. More details can be found in the relevant sections below.

Table 3:

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome / conclusion**
Persistence	Concern confirmed. Conclude L3 is vP based on currently available information on sediment simulation testing OECD TG 308 for L3 and read across to OECD TG 308 for L2.
Bioaccumulation	Concern confirmed. Conclude L3 is vB based on currently available information on bioaccumulation studies OECD TG 305 for L3.
Toxicity	Concern refuted. Conclude L3 is not T based on currently available information on human and ecotoxicological studies with L3.
Suspected vPvB properties	Concern confirmed. Conclude L3 is vPvB as explained above.
Consumer use	Concern refuted No hazards have been identified. Further are human health effects of cosmetics outside the scope of REACH.
Wide dispersive use and exposure of environment	Concern confirmed. Based on use pattern there is wide dispersive use and exposure of the environment.

7.2. Procedure

Octamethyltrisiloxane (L3) 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 for L3 in the conclusion stage. The evaluation of the available test results relies mainly on the UK's assessment and based on this, regulatory actions have been proposed by the Norwegian eMSCA.

Octamethyltrisiloxane (L3) 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), decamethyltetrasiloxane (L4) and dodecamethylpentasiloxane (L5). Data on these substances and on 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.

Information was provided in registration dossiers, publicly available information and information provided to the eMSCA by the Registrant(s). 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 ECHA adopted a decision on 27 March 2017:

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) Exposure assessment and risk characterisation for the 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 the final study report for the OECD TG 308 sediment simulation study for L2. A dossier update containing the requested information on degradation and on exposure information for L3 was received on 25 June 2019 and thereafter the UK eMSCA considered the dossier as completed.

On 9 February 2021, the Registrant(s) provided the 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 in June 2021.

7.3. Identity of the substance

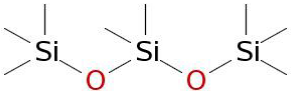
Table 4 displays the identity of the substance according to the ECHA dissemination website.

Table 4

SUBSTANCE IDENTITY	
Public name:	Octamethyltrisiloxane
EC number:	203-497-4
CAS number:	107-51-7
Index number in Annex VI of the CLP Regulation:	n/a
Molecular formula:	$C_8H_{24}O_2Si_3$
Molecular weight range:	236.53
Synonyms:	L3, MDM, Dow Corning 200 (r) fluid 1cst

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

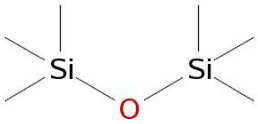
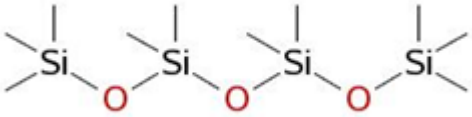
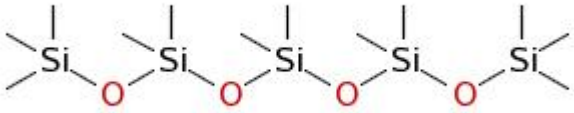
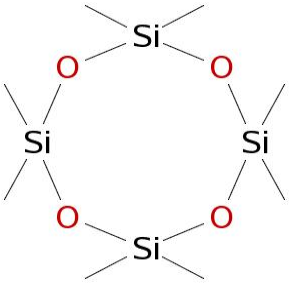
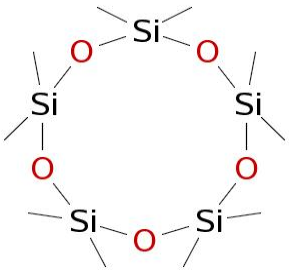
Structural formula:

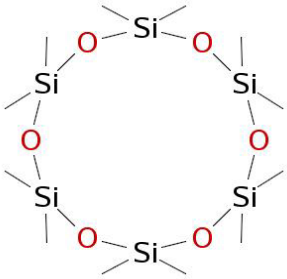


Category information

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	
L4, decamethyltetrasiloxane EC No. 205-491-7 CAS RN 141-62-8	
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	-87.8 °C OECD 102 (DSC)
Boiling Point	152.4 °C OECD 103 (DSC)
Vapour pressure	530 Pa at 25°C OECD 104 (static method Ebuliometer)
Water solubility	0.034 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)	6.6 at 25.3°C OECD 123 (Slow-stirring method)
Partition coefficient n-octanol-air (Log Koa)	3.79± 0.01 at 20.8±0.4°C
Flash Point	31.5 °C at 101.3 kPa Closed cup (ISO 13736:1997)
Explosive properties	Data waiving
Oxidising properties	Data waiving
Stability in organic solvents and identity of relevant degradation products	Data waiving
Dissociation constant	No ionisable groups
Relative density	0.82 at 20°C OECD 109 (oscillating densimeter)
Auto Flammability	340°C at 101.3 kPa DIN EN 14522
Surface tension	Data waiving

7.5. Manufacture and uses

7.5.1. Quantities

The registered aggregated tonnage has increased from 100- 1000 t/a to 1000- 10 000 t/a from 2015 until 2021. 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 L3 on the ECHA's dissemination website.

Table 8

USES	Use(s)
Uses as intermediate	Not listed
Formulation	o Manufacturing and on-site use o Cosmetics, personal care products o Formulation of coatings o Formulation of Health Care application o Non-metal surface treatment agent – 'in-situ treatment' o Formulation of automotive care products o Formulation of adhesives o Formulation or repacking of coatings and paints, thinners, paint removers o Formulation of cleaning agents
Uses at industrial sites	o Industrial use of coating and inks o Industrial use of sealants and adhesives o Use in electronics and optical product manufacturing o Non-metal surface treatment agent – 'in-situ treatment' o Heat transfer fluid o Laboratory chemicals o Cleaning agents
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 consumers has been registered as a new use area. This new use area leads to increased wide dispersal use, professional worker and consumer uses. 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. L3 is an alternative replacement for the

restricted uses of D4 and D5 cosmetic products and the supply volume of L3 has already increased from 100- 1000 t/a in 2015 to 1000- 10 000 t/a in 2021.

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: Notified self-classifications of L3

Number of notifiers	Self-classification
165 (December 2021)	H226: Flammable liquid and vapour.
99 (December 2021)	Not classified
38 (December 2021)	H226: Flammable liquid and vapour. H410: Very toxic to aquatic life with long lasting effects.
17 (December 2021)	H226: Flammable liquid and vapour. H413: May cause long lasting harmful effects to aquatic life.
1 (December 2021)	H226: Flammable liquid and vapour. H304: May be fatal if swallowed and enters airways.
1 (December 2021)	H226: Flammable liquid and vapour. H315: Causes skin irritation. H319: Causes serious eye irritation. H335: May cause respiratory irritation.

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, 2007). The study is given a reliability score of 1. Radiolabelled substances were 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 10. These are for the disappearance of the parent substance.

Table 10:Hydrolysis half-lives of L3

pH	Temperature (°C)	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).
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 relatively long, at around 61 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.

At any given pH the observed first order rate constant (k_{obs}) determined in the study can be expressed by 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 uncatalysed 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 uncatalysed 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+} = 327,000 l $mole^{-1}$ d^{-1} and k_{OH-} = 170,000 l $mole^{-1}$ d^{-1}, both at 25°C[2].

At pH 7, $k_{obs} = k_0 + (327{,}000\times1\times10^{-7}) + (170{,}000\times1\times10^{-7})$.
As k_{obs} at pH 7 and 25°C was determined as 0.0506 d^{-1}, k_0 = 0.0009 d^{-1}.

[2] Very similar values to these are reported in the registration dossier.

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 by using the Arrhenius equation allows value of k_{obs} at any given temperature to be extrapolated[3]. A plot (not shown) of ln k_{obs} versus 1/T (in K) revealed that the activation energy for the reaction was around 68,360 J/mole. The value of k_{obs} at pH 7 can then be estimated to be around 0.0141 d^{-1} at 12°C (equivalent to a half-life of around 49 days) and 0.0103 d^{-1} at 9°C (equivalent to a half-life of around 67 days).

The variation of the k_{obs} at pH values other than 7 is more difficult to estimate as it is not known if the same activation energy would apply to all other pHs[4]. However, as a first approximation the variation of the k_{obs} at other pHs can be assumed to be similar 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 0.0506/0.041 = 3.6 and the value of k_{obs} at 9ºC would be smaller than the value at 25°C by a factor of 0.0506/0.0103 = 4.9).

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, at 25°C, the hydrolysis half-life is predicted to reach a maximum of around 14 days. At 12°C the maximum hydrolysis half-life is predicted to be around 52 days and the half-life is predicted to be above 40 days between a pH of around 6.6 to around 7.3. At 9°C the maximum hydrolysis half-life is predicted to be around 70 days and the half-life is predicted to be above 60 days between a pH of around 6.7 to around 7.2 and is predicted to be above 40 days between a pH of around 6.5 to around 7.5.

[3] 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.

[4] Arrhenius plots for the experimental data at the three temperatures at pH 5 and 9 result in an estimated activation energy of around 53,500 J/mole (pH 5) and 92,100 J/mole (pH 9); the mean of these two values is around 72,800 which is close to the value estimated at pH 7

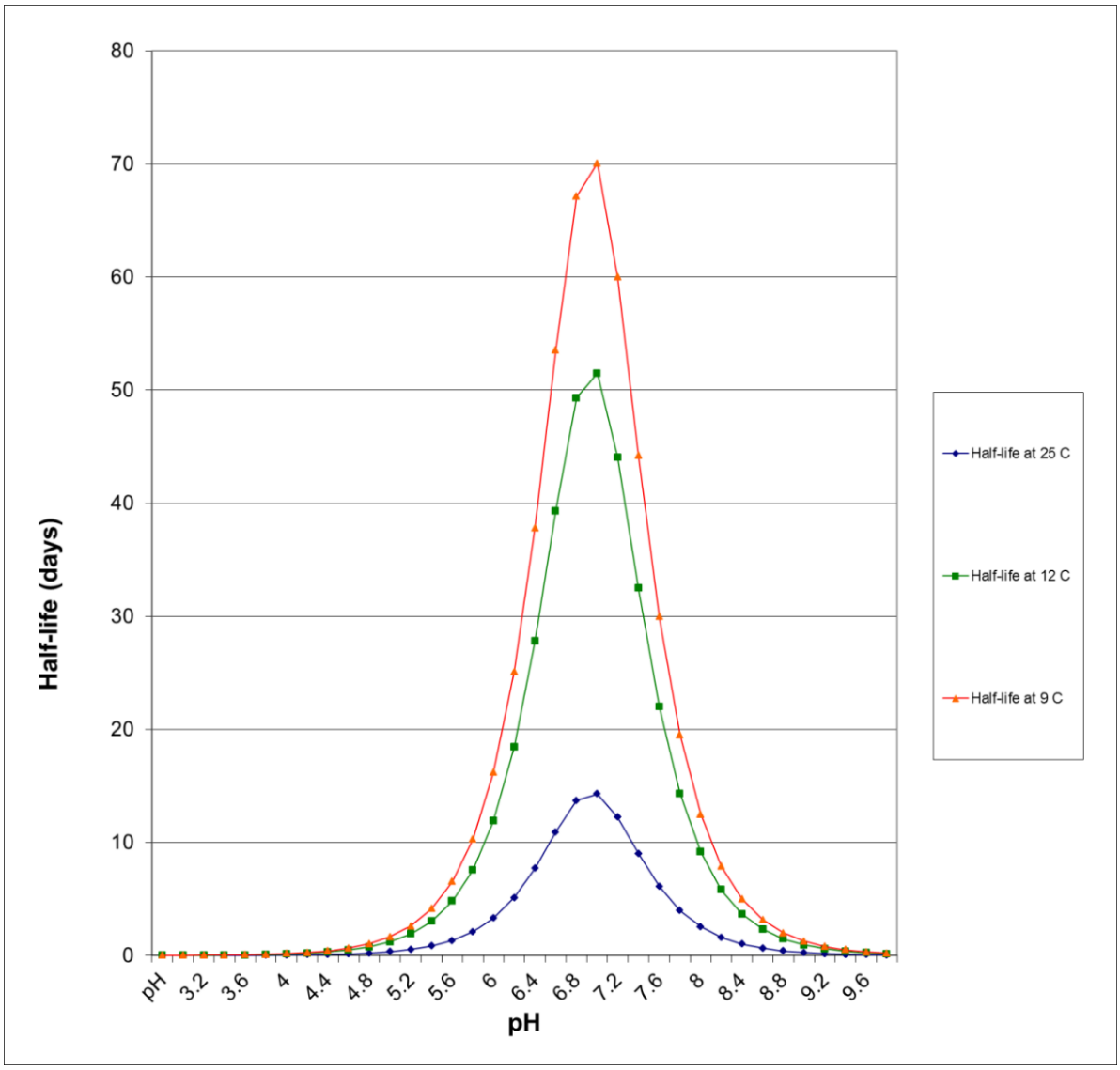


Figure 1: Variation of hydrolysis half-life with temperature and pH for L3

The Registrant(s) have provided additional information (pers. comm, Jan 2016) on this aspect. They calculate that the pH range where the half life exceeds 40 days is between 6.93 and 7.66 at 12°C, with a maximum half life of 55 days occurring at pH 7.3. At 9°C, the 40 day threshold is exceeded between pH 6.79 and 7.89, with the 60 day threshold exceeded between pH 7.02 and 7.65 (maximum half life of 77 days at pH 7.34). 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 E_a values of 53,500 J/mole (pH 5) and 35,500 J/mole (pH 9), which are slightly different to the values used by the eMSCA (see footnote on previous page). 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 0.7 pH units for 12 degrees and 40 days).

In summary, hydrolysis half-lives were determined for L3 using a method in accordance with OECD 111 and in compliance with GLP. The Registrant(s) consider that a hydrolysis half-life of 13.7 days at pH 7 and 25°C demonstrates that the substance is not persistent in the aquatic environment. However, at pH 7 and 10°C a relatively long half-life of around 61 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 52 days at 12 °C.

The hydrolysis rates for the cyclic siloxanes D4 and D5 are also assumed to be impeded by dissolved organic carbon (DOC) (ECHA, 2015). DOC is present in the environment. Therefore, the hydrolytic half-lives for L3 may be longer than suggested by the results in pure water.

No information is available on the potential for hydrolysis of L3 in sediments. It is expected that adsorption onto sediment will reduce the potential for hydrolysis in sediments compared with water, as is the case for some cyclic siloxanes e.g. D4 and D5 (ECHA, 2015).

7.7.1.1.2. Phototransformation / photolysis

7.7.1.1.2.1. Phototransformation in air

No measured data on phototransformation in air are available for L3. The AOPWIN program (v1.92,) has been used to obtain values of the rate constant kOH for reaction of L3 with hydroxyl radicals. The calculated rate constant is 1.2×10^{-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 13 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 is available on phototransformation in water.

7.7.1.1.2.3. Phototransformation in soil

No information is available 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 biodegradation in water have been carried out as adequate experimental data are available.

7.7.1.2.1.2. Screening tests

An OECD Test Guideline 310 ready biodegradability test is reported in the registration dossier for L3 (registration dossier, 2009) and is 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.

Based on this, L3 is not readily biodegradable in a standard screening test.

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

Sediment simulation study on L3 (OECD TG 308)

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

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 11.

Table 11: Characteristics of the two sediments used in the OECD TG 308 study

Property	Calwich Abbey Lake Sediment	Emperor Lake Sediment
% Organic Carbon	4.7% w/w	2.0% w/w
pH (water/0.01M $CaCl_2$)[5]	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 (dw.) Calwich Abbey Lake sediment or 60 gdw. Emperor Lake sediment[6] 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.

[5] pH at Day0, Pre-acclimation pH not available.
[6] Sediment wet weights are quoted as 143 – 151 g Calwich Abbey , and 118 – 122 g Emperor Lake

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%[7] 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 $CaCl_2$) 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

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[8] (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

[7] 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.

[8] 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).

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 12,Table 13 and Table 14 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 12. 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

Table 12: 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 13. 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 13 since the SPE was considered necessary for reliable sample preparation in overlying water.

TMS was the major transformation product (resulting from hydrolysis and identified[9] 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.

Table 13: 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 14 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

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

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 14: Percentage of applied radioactivity associated with the sediment compartment of each test system over the exposure period of the OECD TG 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 3Figure 4). 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 15: Degradation half-lives for L3 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) 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 ECHA's dissemination website for three related substances, the linear siloxane hexamethyldisiloxane or L2 and the two cyclic substances (octamethylcyclotetrasiloxane or D4 and decamethylcyclopentasiloxane or D5). PBT assessments have been performed 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 2018a). The data available for L2, D4 and D5 are summarised in Table 16, along with the data for L3.

Table 16: Comparison of properties of L2, D4 and D5 with L3

Property		Value		
	L3	L2	D4	D5
Molecular formula	$C_8H_{24}O_2Si_3$	$C_6H_{18}OSi_2$	$C_8H_{24}O_4Si_4$	$C_{10}H_{30}O_5Si_5$
Molecular weight (g/mole)	236.53	162.38	296.62	370.8
Water solubility at 23°C (mg/l)	0.034	0.93 mg/L	0.056	0.017
Vapour pressure at 25°C (Pa)	530	5500	132	33.2
Henry's law constant at 25°C (Pa m3 mol-1)	$3.85x10^6$	$0.78x10^6$	$1.21×10^6$	$3.34×10^6$
Henry's law constant at 12°C	$1.62x10^6$	$0.37x10^6$	n.a.	n.a.
log Kow	6.6	5.2	6.49	8.03
log Koc	4.34	3.00	4.22	5.17
Half-life in air (days)	13	11,5	12.7-15.8	10.4
Hydrolysis half-life at pH ~7 (days)	61 at 10°C 52 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)	1180 – 2532 days at 12°C (aerobic conditions)	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 on L2 (OECD TG 308)

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.

L3 has a vapour pressure below that of L2 but has a higher Henry's law constant, which means that L3 has a higher volatility than L2. The potential for adsorption of L3 (as measured by the log Koc) is however higher than L2, which may counteract to some extent the higher volatility of L3 compared to L2 when the whole sediment is considered. Both substances have a similar predicted long residence time in air once volatilised. The hydrolysis half-life in water is longer for L3 than for L2, with 61 days and 17.4 days at 10°C respectively. The hydrolysis half-life in water is longer for L3 than for L2, with 61 and 17.4 days at 10°C respectively.

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 is used in the study. Two sediments were used: Calwich Abbey Lake, UK (silt loam) and Emperor Lake, UK (sandy clay loam). However, the eMSCA 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 THF solvent in order to recover any residual radioactivity.

Table 17 to Table 21 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 17.

Table 17: 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[10] 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 only depicted graphically (and as DPM[11]), it is unclear what proportion of total ^{14}C this represented.

Table 18: 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 19 shows, significant loss of test substance occurred. There was additional uncertainty in the accuracy

[10] No indication was given in the report that a certified analytical reference standards was using to verify this identification
[11] Disintegrations per minute

of the chromatographic profiling because analyses of radioactive content and radioactive purities, pre- and post- dosing of the application solution, were not reported.

Table 19: 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

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 20:.

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 21 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 20: 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 21: 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 Annex XIII persistence criteria for very persistent (vP) are met for L2.

Comparison with D4 and D5

A comparison of the known properties of L3 with those of D4 and D5 reveals that although L3 has a higher vapour pressure than D4 and D5, the Henry's law constant is comparable with between that of D5. A similar volatility from water can thus be expected. All three substances have a similar predicted long residence time in air once volatilised.
The potential for adsorption of L3 (as measured by the log K_{oc}) is between that of D4 and D5. Similarly, the hydrolysis half-life for L3 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 will apply to L3 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 L3 in soil has been carried out (registration dossier, 2010) and is included in the registration dossier. This study used two soils, a Londo soil from Michigan, USA (22% clay, 28% silt, 50% sand, 2.4% organic carbon) and a silty loam from Buxton, UK (22% clay, 56% silt, 22% sand, 3.4% organic carbon). The test substance used was radiolabelled (mostly on the dimethylsiloxyl moiety) and had a radiochemical purity of 99.1%.

For the experiments, 5 g of air-dried soil was added to pre-weighed 25 ml Teflon tubes. The dry soil in the tubes was pre-conditioned for at least a week in containers with controlled humidity atmosphere (humidity levels of the air 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 experiments were placed into controlled humidity chambers. The majority of the experiments were conducted at 22.5°C; for the Londo soil, experiments in closed systems were also conducted at 4°C and 38.5°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 99.1 to 100.8%. Up to one third of the substance was lost in the open system experiments at 92% RH, and over 95% was lost at 100% RH (the half-life for volatilisation at 100% RH was less than one day). Volatilisation was not significant at 32% RH.

The half-lives determined for the dissipation of the parent substance in the Londo soil at 22.5°C are shown in Table 22.

Table 22:Degradation half-lives of L3 in soil

Relative humidity of air (%)	Half-life (days) at 22.5°C
100	119.5
92	6.19
42	3.62
32	1.47

In the silty loam soil the half-life at 22.5°C and 32% relative humidity was 1.47 days.
Experiments in the Londo soil were also carried out at different temperatures at a relatively humidity of 42%. The half-life was determined as 19.9 days at 4°C, 3.62 days at 22.5°C and 0.96 days at 38.5°C These results show a clear temperature dependence in the degradation.

The following degradation products were identified: dimethylsilanediol; trimethylsilanol; and 3,3,3,1,1-pentamethyldisiloxanol. 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 of the air. The nature of the non-extractable fraction was not completely understood but it was thought that the non-extractable fraction may be strongly adsorbed diols.

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) give it a reliability score of 2.

The results of this test show that L3 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 100% relative humidity air the half-life approached 120 days at 22.5°C.

7.7.1.3. Summary on degradation

L3 is predicted to degrade in the atmosphere as a result of reaction with hydroxyl radicals. The half-life for L3 in the atmosphere is approximately 13 days.

The substance is not readily biodegradable in aquatic systems, but does undergo hydrolysis to some extent. The hydrolysis half-life is dependent on the pH and temperature. At pH 7

it reached a maximum of 14 days at 25°C, 52 days at 12°C and 61 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 L3 may therefore be longer than suggested by the results in pure water.
L3 is a volatile substance and loss by volatilisation would also be likely to occur alongside degradation in water and soil systems.

In a sediment simulation study with L3 (OECD 308), the calculated half-life was 6.91 years in Calwich Abbey sediment and 3.5 years in Emperor Lake sediment at 12°C.

Degradation of L3 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 L3 in soil may, under some circumstances, be relatively short (half-life of a few days) but may under other environmental conditions be expected to be relatively long (120 days). The study is however not easily interpreted and has several flaws.

7.7.2. Environmental distribution

7.7.2.1. Absorption / desorption

A log Koc has been determined from three soils in an OECD 106 study. The average of the three results is log K_{oc} = 4.34 and the individual values log K_{oc} were 4.28, 4.37 and 4.38. The Registrant(s) comment that the similarity of Koc value and isotherms derived in the test indicates that partitioning into soil organic matter dominated the overall sorption from water.

7.7.2.2. Volatilisation

L3 has a relatively high vapour pressure (530 Pa at 25ºC) and low water solubility (0.034 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 3.59×10^6 Pa m^3/mole at 25ºC and 1.72×10^6 Pa m^3/mole at 12ºC. Furthermore, the dimensionless Henry's law constant (K_{aw}) can be estimated as 1,449 at 25°C and 725 at 12°C.

Values for the Henrys law constant is also available in the registration as 2.68×10^6 Pa m^3 mol^{-1} at 20.8°C and 1.62×10^6 Pa m^3 mol at 12°C, based on a Log K_{AW} of 3.04. The Log K_{AW} value was 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 3.85×10^6 Pa m^3 mol^{-1} at 25°C can also be determined from this Log K_{AW} of 3.04. The calculation was performed by the eMSCA using a basic temperature correction equation[12] and assumes the same enthalpy of water-air phase change (dU_{AW}) 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 very close to the value estimated using the EUSES program.

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 compartments has been estimated using the SimpleTreat model (implemented in EUSES 2.1.2).

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

Table 23: Distribution modelling for STP

Fraction of emission directed to:	%
Air	44.4
Water	3.5
Sludge	52
Degraded	0

Air and sludge are the main compartments, with partitioning to water also being significant. Compared to L4, there is a significant difference between the proportion to air and to sludge modelled for L3, with higher levels of L3 in air and lower levels in water and sludge.

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[13].
In order to assess the effects of the uncertainties in several parameters (notably the rate of degradation in soil and rate of hydrolysis) the modelling was carried out several times using different assumptions for these two parameters. The inputs used and the resulting modelled outputs are summarised in Table 24.

For all estimates the molecular weight was set at 236.53 g/mole, the degradation half-life in air was set at 312 hours (13 days), the log Kow was set at 6.6 and the log Kaw was set at 2.86 (K_{aw} = 725). 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. This 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.

It is also relevant to note that the substance is predicted to have a relatively long overall persistence (Pov) for emission to water. 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 L3.

Table 24: Summary of long-range transport potential estimated using the OECD Pov and LRTP screening tool

13

Input assumptions		Modelled outputs		
		Pov (days)[1]	CTD (km)[2]	TE (%)[3]
Half-life in soil = 4,800 hours (200 days)		70 (water)	6,451	0.024
		63 (water)	6,451	0.024
		48 (water)	6,451	0.024
Half-life in soil = 2,880 hours (120 days)		70 (water)	6,451	0.024
		63 (water)	6,451	0.024
		48 (water)	6,451	0.024
Half-life in soil = 1,128 hours (47 days)		70 (water)	6,450	0.024
		63 (water)	6,450	0.024
		48 (water)	6,450	0.024
Half-life in soil = 240 hours (10 days)		70 (water)	6,449	0.024
		63 (water)	6,449	0.024
		48 (water)	6,449	0.024

Notes:

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

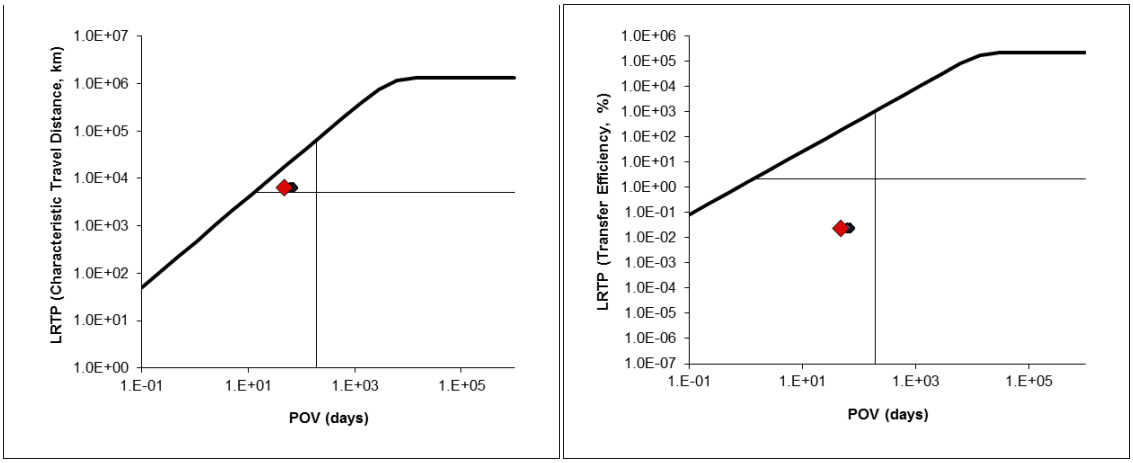


Figure 4: Long-range transport potential of L3

As sorption to particles in air are not likely to be significant for chemicals with a low log K_{OA}[14], 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 L3.

In summary, L3 has a potential for long-range transport via the atmosphere but a low potential for subsequent (re-)deposition in remote areas.

[14] Log Koa (KOAWIN v1.10 estimate): 4.473

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 L3 in fish, according to OECD test guideline 305 that was performed in compliance with GLP (registration dossier, 2006). Fathead minnows (*Pimephales promelas*) were used, with an average wet weight of 1.32 g at the start of the test and an average length of 58 mm. The test was conducted under flow through conditions, in 57 liter polyethylene aquaria containing approximately 42 litres of test medium using a replacement rate of 10 volume additions per day. The mixing chambers were sealed to prevent volatilisation of the substance.
Stock solutions of the ^{14}C-labelled substance in dimethylformamide were made. Two test concentrations were used, nominal levels 3.4 and 34 µg/l, mean measured concentrations 1.7 and 21 µg/l. The duration of the uptake phase of the test was 42 days, with sampling on days 0, 3, 7, 14, 21, 28, 35 and 42. The depuration phase was 10 days, with sampling on days 1, 3, 7 and 10. The concentration of the substance was measured on a whole fish basis, and in water samples taken 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 in the 1.7 µg/l exposures, and at 21 days in the 21 µg/l exposures. The BCF values based on the steady state concentrations in fish and in water were 5,030 l/kg (1.7 µg/l exposure) and 7,730 l/kg (21 µg/l exposure). Kinetic parameters were also determined from the test results. In the 1.7 µg/l exposure, the uptake rate (k_1) was 1,210 l kg^{-1} d^{-1}, and the depuration rate (k_2) was 0.336 d^{-1}, resulting in a kinetic BCF of 3,610 l/kg. In the 21 µg/l exposure, k_1 was 1,040 l kg^{-1} d^{-1}, k_2 was 0.186 d^{-1}, and the kinetic BCF was 5,600 l/kg. The mean lipid content of the fish was 3% at test initiation and 1.3% at test termination.

The percentage of radioactivity in the fish associated with the parent substance L3 was 97.7% on average. The percentage associated with an unknown metabolite was 1.4%, and the percentage of radioactivity not extracted was 0.9%

The validity criteria for the test were met and Registrant(s) gave a reliability score of 1.
The study has been evaluated by the eMSCA and is considered valid. However, there are a few issues to the study that warrant further consideration:

- The fish used in the test had lipid contents of 3% at the start of the study and 1.3% at the end of the study (the average lipid content would be around 2.2%). 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 11,430 l/kg (1.7 µg/l exposure) and 17,570 l/kg (21 µg/l exposure). Similarly. the kinetic BCF_L would be around 8,200 l/kg (1.7 µg/l exposure) and 12,730 l/kg (21 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 were up to a factor of 4 or more at some time points during the uptake period and a factor of 10 or more during depuration. This means that there is some uncertainty over 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 presented in the registration dossier have been re-analysed using the sequential method.

The concentration data are summarised in Table 25 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 and 28 for the 1.7 µg/l treatment group and days 21, 28 and 42 for the 21 µg/l treatment group. There is no discussion in the registration dossiers on why data for different times were used for the two treatment groups and, in particular, why the day 35 data (both treatment groups) and day 42 data (1.7 µg/l group) were not included in calculating the average steady state concentration. The steady state concentrations that can be estimated from the data are summarised below, along with the estimated standard deviation.

1.7 µg/l treatment group

Mean fish concentration based on day 14, 21 and 28 values (as assumed in the registration dossier): 8,543 ± 3,490 µg/kg.

Mean fish concentration based on all samples between day 14 and 42: 6,694 ± 3,565.

The standard deviation around the mean measured water concentration of 1.7 µg/l was ±0.2 µg/l. Thus, the BCFs (± standard deviation) that can be estimated from the above two steady state concentrations are as follows.

Mean steady state BCF based on day 14, 21 and 28 values (as assumed in the registration dossier): 5,030 ± 2,140 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 11,430 ± 4,860 l/kg.

Mean steady state BCF based on all samples between day 14 and 42: 3,940 ± 2,150 l/kg (not lipid normalised). Ignoring the uncertainty in the lipid content, the lipid normalised BCF_L would then be 8,950 ± 4,890 l/kg.

21 µg/l treatment group

Mean fish concentration based on day 21, 28 and 42 values (as assumed in registration dossier): 162,226 ± 58,096 µg/kg.

Mean fish concentration based on all samples between day 21 and 42: 137,898 ± 66,248.

The standard deviation around the mean measured water concentration of 21 µg/l was ± 1.7 µg/l. Thus, the BCFs (± standard deviation) that can be estimated from the above two steady state concentrations are as follows.

Mean steady state BCF based on day 21, 27 and 42 values (as assumed in registration dossier): 7,730 ± 2,840 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 17,570 ± 6,450 l/k g.

Mean steady state BCF based on all samples between day 21 and 42: 6,570 ± 3,200 l/kg (not lipid normalised). Ignoring the uncertainty in the lipid content, the lipid normalised BCF_L would then be 14,930 ± 7,270 l/kg.

Thus, leaving out some of the results from day 35 and day 42 (lower concentration only) reduces the standard deviation around the BCF, and also increases the magnitude of the BCF. This probably does not reflect the true uncertainty in the steady state BCF. Nevertheless, all the steady state BCFs, regardless of which data are used to estimate the steady state concentration, are >5,000 l/kg when lipid normalised.

- The variability in the measured concentrations in fish is also a relevant consideration 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 as the uncertainty in the value of k_2 obtained 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 first 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 25: Summary of concentrations measured in fish during the BCF study

Day	Concentration in fish (µg/kg)[a]	
	1.7 µg/l treatment group	21 µ/l treatment group
Uptake		
0	169; 130; 120; <LOQ	829; 893; 1,379; 659
3	5,552; 4,100; 2,150; 3,840	29,978; 41,614; 28,960; 46,081
7	4,544; 4,482; 7,118; 3,242	90,966; 75,402; 111,957; 77,535
14	10,380; 13,453; 5,711; 3,177	146,348; 107,023; 141,739, 87,103
21	12,738; 9,096; 9,722; 11,329	154,362; 121,214; 157,552; 70,150
28	9,631; 9,045; 3,107; 5,130	234,315; 136,078; 201,974; 225,015
35	5,329; 4,694; 3,271; 3,018	74,898; 52,501; 61,638; 70,620
42	4,500; 3,064; 3,636; 3,857	59,225; 215,634; 164,083; 207,111
Depuration		
43	3,062; 4,197; 3,320; 3,079	52,835; 62,826; 72,766; 72,986
45	1,201; 2,111; 1,311; 1,184	25,803; 41,602; 36,285; 43,388
49	396; 501; 491; 469	22,456; 6,643; 97,873; 15,930
52	123; 91.5; 124; 949	6,077; 19,467; 4,074; 17,098

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

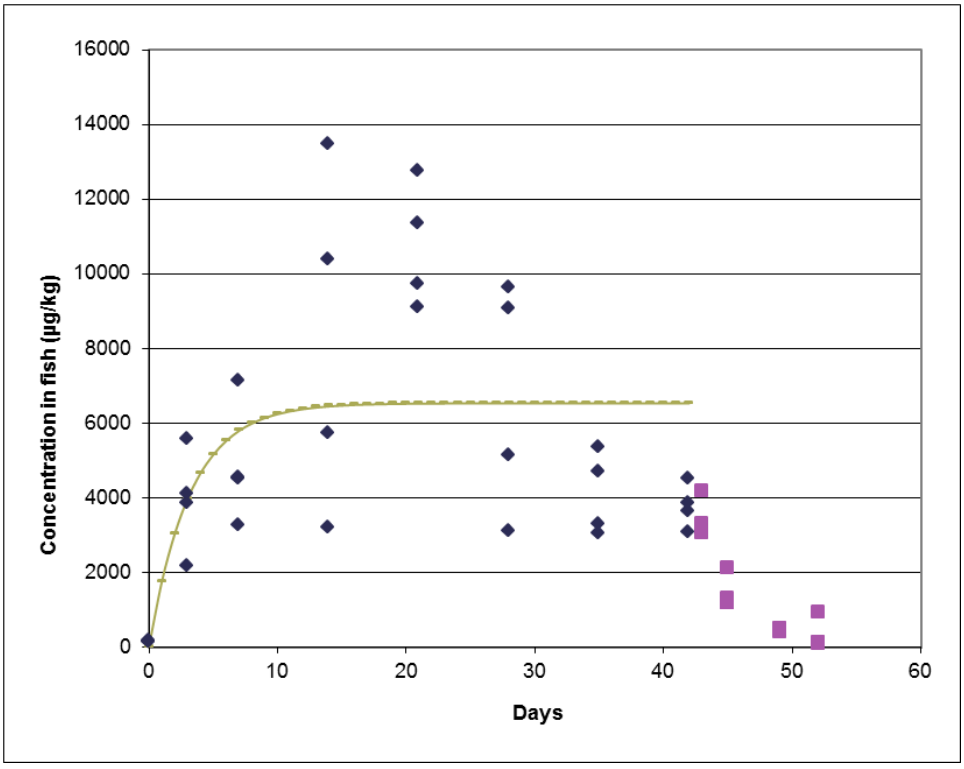


Figure 5: Plot showing the fish bioconcentration data for the 1.7 µg/l treatment group

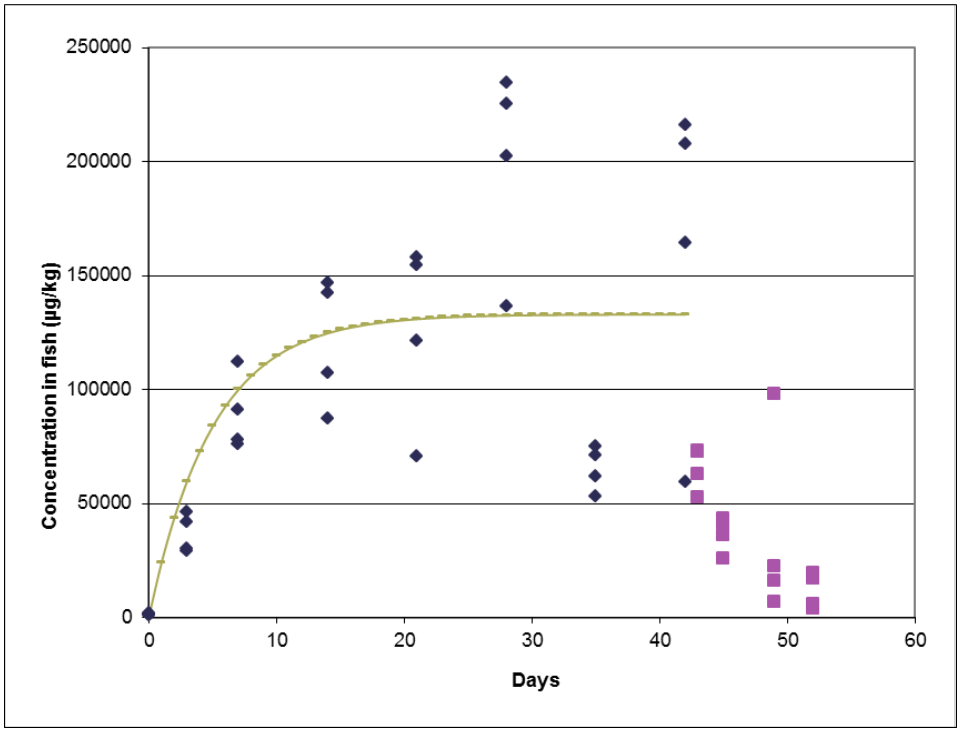


Figure 6: Plot showing the fish bioconcentration data for the 21 µg/l treatment group

1.7 µg/l treatment group

k_2 = 0.311 d^{-1} (see Figure 7). The R^2 value of the regression plot was 0.83 and the slope of the plot was statistically significantly different from zero ($p<0.05$). The standard error in the k_2 value was ±0.038 d^{-1}.

The value of k_1 obtained from least squares fitting of the uptake curve[15] was 1,196 l kg^{-1} d^{-1}, resulting in a kinetic BCF of 3,845 l/kg. Lipid normalisation of this value results in a BCF of 8,740 l/kg. These values are very similar to those reported in the registration dossier obtained by the simultaneous method.

21 µg/l treatment group

k_2 = 0.199 d^{-1} (see Figure 8). The R^2 value of the regression plot was 0.56 and the slope of the plot was statistically significantly different from zero ($p<0.05$). The standard error in the k_2 value was ±0.047 d^{-1}.
The value of k_1 obtained from least squares fitting of the uptake curve was 1,257 kg^{-1} d^{-1}, resulting in a kinetic BCF of 6,320 l/kg. Lipid normalisation of this value results in a BCF_L of 14,360 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.

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

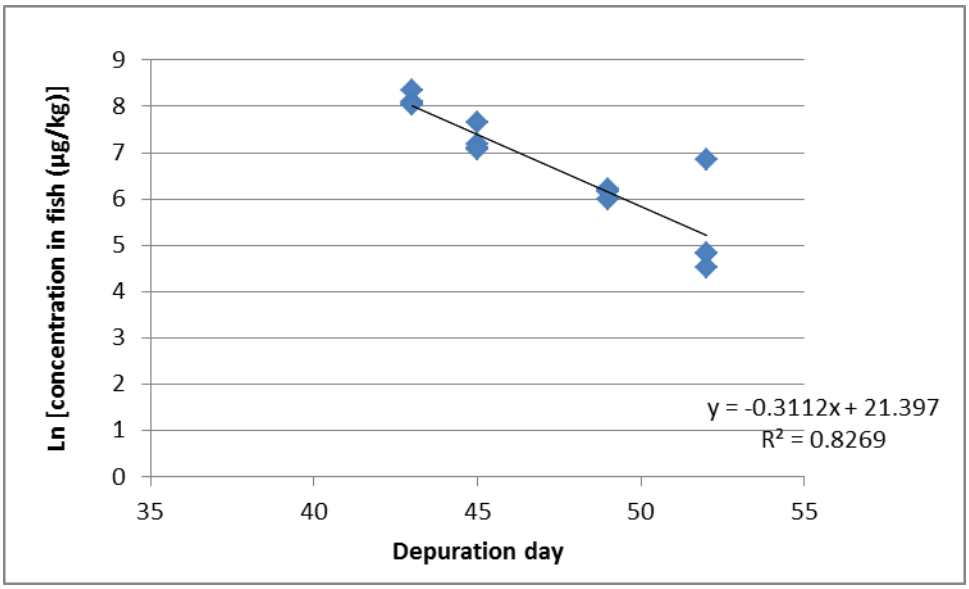


Figure 7: Plot of ln [concentration in fish] versus time for the1.7 µg/l treatment group

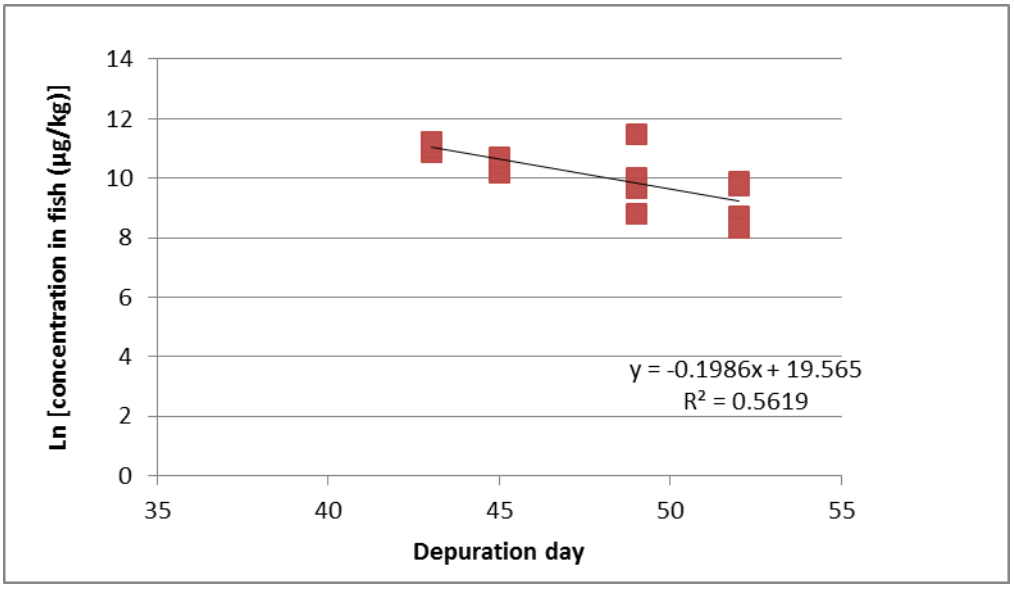


Figure 8: Plot of ln [concentration in fish] versus time for the21 µg/l treatment group

Overall, although there is some uncertainty over this study resulting from the variability in the data at some time points, the results show that L3 has a BCF value >5,000 l/kg. Although some methods for estimating the BCF at the lowest exposure concentration result in values lower than 5,000 l/kg (in the range 3,610 to 3,940 l/kg depending on how the data are analysed), the BCFs obtained at the higher exposure concentration were all >5,000 l/kg (in the range 5,600 to 7,730). The fish used in the study had a relatively low lipid content (around 1.9% - see discussion below). When the BCF is normalised to a lipid content of 5% all methods for estimating the BCF from the data result in BCF values >5,000 l/kg. The range of values for the lower exposure group is 9,500 to 10,368 l/kg and for the higher exposure group is 14,737 to 20,342 l/kg, depending on how the data are analysed.

Although the BCF value is relatively high for L3, the substance also depurates reasonably rapidly from the fish (as evidenced by the fact that the k_2 value is around 0.19-0.34 d^{-1}), giving a clearance half-life of between 2 and 4 days. Normally substances with a k_2 above 0.15 day^{-1} would not be expected to exhibit a BCF above 2,000 l/kg (Brooke and Crookes, 2012). However, in this case the substance has an uptake rate constant that is higher than

expected[16]. In addition, 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.
There was no significant growth of the fish during the test, in either the control group or the exposed groups.

The fish lipid content declined slightly during the test. The mean (±standard deviation) lipid contents were 3.0% at the start of the test, 1.4% at day 42 and 1.3% at day 52. The mean lipid contents represent those in the controls and exposed groups combined (2 fish from each group were sampled at each time point). The overall average fish lipid content (average of days 0, 42 and 52) is 1.90±0.95%.

7.7.3.1.2. Dietary study

A dietary accumulation study with rainbow trout (*Oncorhynchus mykiss*) has been undertaken with L3 (registration dossier, 2010b). The test was carried out broadly in line with the OECD 305 Test Guideline and used a 35 day uptake period followed by a 30 day depuration period. A 3% feeding rate was used in the test, and the food during the uptake period contained 436 µg/g L3. Prior to the start of the test, the fish had an average length of 44 mm (range 39 to 51 mm) and an average weight of 0.64 g (range 0.46 to 0.92 g).
The exposed fish minus the gastrointestinal tract were analysed in order to avoid potential complications from the presence of undigested food during the uptake phase. During the depuration phase the liver was also removed and analysed separately.

Steady state was reached in the fish by day 21 of the test (the concentrations measured in the fish at days 21, 28 and 38 were not significantly different ($p>0.05$)). The mean steady state concentration in the fish over this time period was determined to be 45.9 µg/kg, giving the steady state BMF as 0.11. Comparison of the concentrations determined by parent compound analysis with those obtained by total ^{14}C analysis indicated that the majority of the radioactivity present at steady state was essentially the parent compound. However, analysis of the liver during depuration indicated the presence of one or more metabolites.
The mean lipid content of the food used in the test was 17.9% (standard deviation 0.19%). The arithmetic mean lipid content of all the fish values determined was 5.0% (standard deviation 1.9%).

Overall, this study shows that the lipid normalised BMF for L3 is <1. It should be noted, however, that L3 was added directly to the fish food and no positive control was used in the test. Therefore, the appropriateness of the method of preparation of the test food cannot be established.

7.7.3.1.3. Other information

In the registration dossier the Registrant(s) cite the ECHA PBT guidance (ECHA, 2017) suggesting that valid BCF values may not be possible for low solubility chemicals from aqueous fish bioconcentration studies, due the difficulty in maintaining test substance concentration. In response, ECHA notes that there is no indication that there was a problem in maintaining the exposure of L3. 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*.

Furthermore, the Registrant(s) state that steady state may be difficult to achieve for highly lipophilic and adsorbing substances. However, the fish bioconcentration robust study summary in the registration dossier states that steady state was reached at day 14 (lower concentration) and day 21 (higher concentration).

[16] For example using the method Sijm *et al.* (1995) given in the REACH guidance, the k_1 value predicted for fish of weight 1.32 g would be 476 l kg^{-1} d^{-1} which is much lower than determined in the experiment (1,040 to 1,257 l kg^{-1} d^{-1}).

The Registrant(s) explain that this is because the subsequent fish concentrations measured after those times were not statistically different. Therefore, reaching steady state does not appear to be an issue for the L3-study. In any case, as a kinetic BCF (both significantly exceeding 5000) is derived, achievement of steady state is not essential to reach a conclusion in this case.

In the PBT assessment, the Registrant(s) also comment that the food in the dietary study was highly dosed (436 µg/g mean measured concentration of radio labelled L3), which may limit the applicability of the values obtained. It is unclear what this means, as the concentration would be within the recommended range in the OECD 305 test guideline of 1 – 1000 µg/g for substances without a specific toxic mechanism.

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. The Registrant(s) argue that these are more reliable metrics as they are *independent of the exposure concentration and route of exposure*. eMSCA is unclear why these issues are a concern in this instance. 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 eMSCA the BCF value is a result that should be taken from the test for comparison with the Annex XIII criteria. The eMSCA would agree that interpreting a fish dietary study with respect to the Annex XIII criteria is more challenging, and note that the draft 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) argue 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. It is therefore not appropriate to derive a single half-life applicable across all species. In the MSC opinion (ECHA, 2015) 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, it does not take into account 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 1 when the elimination half-life was as short as 7.7 days. These 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 depend on the fish size. The uptake rate constant can vary with size and 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 a 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 a (lipid normalised) k2 value below 0.085 d^{-1} (ie. 8.2 days) is comparable to a BCF exceeding 5000. This is considerably shorter than the 70 days ascribed by Goss et al. (2013). 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 also notes that the k2 calculated in the fish feeding study is 0.045 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 determine fugacity ratios (F/R) for L3 based on the measured log Kow (6.6) 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 0.06 to 0.13 for L3. The Registrant(s) state 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 lipid-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 L3, the high log Kow value (6.6, OECD 123) is a further reason that the F/R value is relatively 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 indicate 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 the biomagnification potential.

The eMSCA notes that in the case of another siloxane (D5), the fish BCF values exceeded 5000, the 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 20,342 are in contrast to the low levels of accumulation that are suggested by the fugacity ratios.

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

The BCF for L3 in fathead minnow (*Pimephales promelas)*, has been determined to be in the range 9,500 to 20,342 l/kg, when normalised to a 5% lipid content. The study was well carried out but there was some variability between the concentrations measured within replicates at some time periods, which means that there is some uncertainty as to the precise BCF for L3 from this study. Despite this, the weight of evidence drawn from this study is that the BCF for L3 is >5,000 l/kg.
The results of a dietary bioaccumulation study are also available for L3 with rainbow trout (*Oncorhynchus mykiss)*. This study shows a lipid-normalised steady-state BMF value of 0.38 and a lipid-normalised kinetic BMF value of 0.45. eMSCA does not consider that a BMF from a fish feeding study is equivalent to a field BMF. This is due to the fact that the only

contaminant exposure is via food, and the fish exist in clean water, potentially allowing greater depuration to the media during uptake. This means that a dietary BMF close to, but below, 1 can still indicate equivalence to a BCF of above 2000 or 5000 L/kg.

While the eMSCA note the theoretical outcome of the F/R calculation, the available measured data in whole animals should be preferred. The F/R ratios are not yet accepted for REACH purposes. In this case, the (lipid normalised) BCF values of up to 20,342 are in contrast to the low levels of accumulation that are suggested by the fugacity ratios.

7.7.4. Environmental monitoring data

In a compilation of Norwegian monitoring from 2002 – 2012[17] (Arp, 2012), L4 was detected more frequently than L2 and L3, but less than the cyclic siloxanes D4-D6. L3 was not detected above the LOD in fresh/marine water, nor in freshwater/marine sediment (7 and 3 samples respectively). It was, however found in WWTP sludge and water, (3 samples, 3 detections, max 31 ng/g dw, 5 samples, 1 detection max 32 ng/l) from monitoring performed in 2005 and 2007. A number of biota were also sampled: Cod liver (21 samples, 4 samples above the l.o.d. max 0.33 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 L3. In samples collected in 2016, the linear siloxanes were detected in all samples of indoor air, house dust and sewage sludge. L3 was detected in sewage sludge (2,2-7,3 ng/g), house dust (0.23 – 1.3 ng/m^3) indoor air (1.6 – 743 ng/m^3) and brown trout (0,05 ng/g) but not in samples from rat, landfill leachate or surface water (Schlabach et al., 2017) 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 L3 in inlet wastewater (COWI 2018) in samples from 2017.

In samples collected in 2018, the linear siloxanes were detected in all selected sample types, including indoor environments. L3 was found in most samples of sewage water (3.1 – 28 ng/L) and house dust (2.1 – 261 ng/m^3) and at a low frequency in sediment samples (0.06 ng/g), but not in gull eggs or blue mussels (Schlabach et al., 2019). The results from the studies demonstrate lower detection frequencies and levels of L3 compared to L4 and L5.

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 (l.o.d. 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. Please note that the samples collected in 2004 were analysed in 2008.

[17] This includes data from a further citation: Green, N., Schlabach, M., Strand, A., Schøyen, M., Kaj, L. 2007. Siloxanes in the environment of the Inner Oslofjord. Report 986/2007. TA2269. Norwegian Pollution Control Authority (SFT).

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 samples, 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) conducted a wider analysis of siloxanes in the Nordic countries. This project included monitoring of air (24, l.o.d. 0.006 ug/m3), 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 (14ng/g dw), and biota samples. The biota samples consisted of composite samples of livers of different fish species (21), seabird eggs (17), and cetacean blubber (7). L3 was not detected in any of the biota, air, sediment or natural water samples. It was detected in two of the samples from STP influents (0.0034 – 0.014 µg/l). 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 in some industrial effluents. It was also 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, in some landfill and STP influents and in one STP effluent (<l.o.d – 0.041 µg/l). It was not detected in any of the biota samples.

As part of routine monitoring (McGoldrick et al, 2014), 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. L4 was not detected in any of the 87 fish caught (detection limit, DL, 0.31 ng/g w/w), and neither were L2 (HMDS, 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 (*Euphausiacea*) 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. 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) appear to be legitimate and therefore the data are not taken into account for the further assessments 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 (this 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.

L3 has recently been analysed in sewage sludge in Norway (Blytt and Stang, 2018). In 70 sludge samples collected across a total of 10 STPs, L3 was detected in 15 of the samples. The range of concentration was below l.o.d (0.020 mg/kg) to 0.07 mg/kg., but with a increasing trend. In a similar campaign from 2013, L3 was also detected, with lower frequency but the same concentration range (Blytt et al., 2013). L2 and L4 were also monitored, together with other cyclic siloxanes.

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 L3, 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 a 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 the detection limit (0.082, 0.09 and 0.091 µg/l) in both influent and effluent water samples. 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, the concentrations of the cyclic siloxanes were significantly higher.

Olofsson et al. (2012) reviewed trends of L3, L4 and L5 different contaminants 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 17 siloxanes at 42 wastewater treatment plants across 23 cities in China from samples of anaerobic digested sludge after the dewatering process. The sites 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 13 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.

Sanchis 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.

The influent samples showed that the main compounds were cyclic siloxanes and L5. L5 was the most frequently found compound and was detected in all 15 WWTP influents in higher concentrations than for L4., L3 was only above the method limit of quantification (MloQ) in four, and detectable but not quantifiable in a further three. 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 11 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., 2015). 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. Pine needles were used as biomonitor of airborne persistent organic pollutants. Analytical recoveries across the three matrices was similar, but varied for the different chemicals 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 wintertime in Porto (actual sample type not specified). The linear siloxanes were detected at a 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

[18] Sorbent-impregnated polyurethane foam [disks]

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 L3 in the environment. Where sewage sludge has been monitored, L3 can generally be detected, albeit at ng/g levels. Given the use in cosmetic and automotive care products and the lack of biodegradability, detection at STPs is expected. In recent screening campaigns in Norway, L3 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 the supply volume of the linear siloxanes compared to the cyclic siloxanes. Although D4 and D5 are registered at much higher volumes than L3, several uses of D4 and D5 have been restricted. Increasing supply volumes can therefore be expected for L3 since it is an alternative compound for the restricted uses of D4, D5 and D6. Therefore, higher concentrations of L3 in the environment can be expected in future.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

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 26**.** The substance is not acutely toxic to fish at concentrations up to the limit of solubility in the test medium.

Table 26: Summary of short-term toxicity of L3 to fish

Species	Value	Remarks	Reference
Oncorhynchus mykiss	96h-LC_{50} > 19.4 µg/l	OECD TG 203, reliability score 1. Measured concentration (nominal 34 µg/l)	Registration dossier (study report, 2007)

7.8.1.1.2. Long-term toxicity to fish

The long-term toxicity data for fish given in the registration dossier are summarized in Table 27. The substance is not toxic to fish over longer-term exposure at concentrations up to the limit of solubility in the test medium.

Table 27: Summary of long-term toxicity of L3 to fish

Species	Value	Remarks	Reference
Rainbow trout (*Oncorhynchus mykiss)*	90d-NOEC ≥ 27 µg/l	Fish, Early-Life Stage (FELS) test, OECD TG 210. OECD TG 210, reliability score 1. Endpoints embryo survival, larval hatch and growth. Measured concentration (nominal 34 µg/l)	Registration dossier (study report, 2010)
Fathead minnow *(Pimephales promelas)*	35d-NOEC ≥ 21 µg/l	Results from OECD TG 305 bioconcentration test, reliability score 1. Endpoint mortality. Measured concentration (nominal 34 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)
Oncorhynchus mykiss	14d-NOEC ≥ 34 µg/l	OECD TG 204, reliability 2. Endpoint mortality, length and weight. Nominal concentration. Not to GLP	Registration dossier (study report, 2009)

For the FELS test, the results are quoted as time-weighted means. The highest concentration was nominally 34 µg/l, which is the limit of water solubility. In the test, the time-weighted mean for this treatment was 27 µg/l indicating that saturation was achieved. The registration dossier states that there were no statistically significant treatment related effects and the eMSCA agrees with this conclusion.

In the fish bioconcentration test using L3, 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.

One further test included in the registration dossier is an OECD 204 prolonged fish toxicity test. No statically significant effects up to the limit of solubility were observed (lethality or length/weight changes). There was no chemical analysis in the test so results are based on nominal concentrations. Flow-through conditions were used. The Registrant(s) include the data as supporting information, and the eMSCA agrees with this. Similar to the bioconcentration study, the lack of effects are consistent with the FELS test.

7.8.1.2. Aquatic invertebrates

7.8.1.2.1. Short-term toxicity to aquatic invertebrates

The short-term toxicity data to aquatic invertebrates given in the registration dossier are summarized in Table 28. The substance is not acutely toxic to aquatic invertebrates at concentrations up to the limit of solubility in the test medium.

Table 28: Summary of short-term toxicity of L3 to aquatic invertebrates

Species	Value	Remarks	Reference
Daphnia magna	48h-EC_{50} > 20 µg/l	OECD TG 202, reliability score 1. Endpoint mobility. Measured concentration (nominal 34 µg/l)	Registration dossier (study report 2007)

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 29. 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 29: Summary of long-term toxicity of L3 to aquatic invertebrates

Species	Value	Remarks	Reference
Daphnia magna	21d-NOEC ≥ 14.3 µg/l	OECD TG 211, reliability score 1. Endpoints growth, reproduction. Measured concentration (nominal 34 µg/l)	Registration dossier (study report 2010)

The eMSCA notes 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 30. The substance is not toxic to algae at concentrations up to the limit of solubility in the test medium.

Table 30: Summary of toxicity of L3 to algae

Species	Value	Remarks	Reference
Pseudokirchneriella subcapitata	72h-NOEC ≥ 9.4 µg/l	OECD TG 201, reliability score 1. Endpoint growth rate. Measured concentration (nominal 34 µg/l)	Registration dossier (study report 2009),

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 registration dossier contain five studies with sediment organisms in a weight of evidence approach. Toxicity was observed in two of the five toxicity tests.

There is some variation between the three *Lumbriculus* studies. The Registrant(s) have noted some issues with the 2009 study in the registration dossier. The *Lumbriculus* study from 2009 derives the lowest NOEC of all sediment test with L3. The Registrant(s) state that there are a number of possible contributing factors that could have caused higher toxicity in this study.

In the 2009 study is it is thought that the artificial sediment with peat based carbon source and high pH values interfered with the test system to exhibit toxicity that is mediated by the interaction of the substance with components of artificial sediment with peat based carbon source at high pH. The peat content of this study was higher than recommended 4-5 % in the OECD 225 TG. The pH of other available *Lumbriculus* study using artificial

sediment was similar, but the peat content was in accordance with the recommendations in the TG (5 %) and no effects were observed in this study.

Furthermore, in both the Lumbriculus studies from 2013 and 2017, the worms were synchronised prior to testing, whereas the worms in the study from 2009 were not. This can lead to variability in reproduction and difficulty in interpreting results.

The reproduction was quite poor in the 2009 study, with the number of worms at the end of the study (day 28) in the control vessels not quite meeting the validity criteria outlined in the OECD TG 225 guidance (the average number of living worms per replicate in the controls should have increased by a factor of at least 1.8 at the end of exposure compared to the number of worms per replicate at the start of exposure; the worms in the 2009 study increased by a factor of 1.73). Although this slight difference in reproductive increase might not lead to disregarding of the study, the combination of factors discussed above indicates that this study is less reliable than the 2013 and 2017 studies.

Table 31: Summary of toxicity of L3 to sediment organisms

Species	Value	Remarks	Reference
Chironomus riparius	28d-NOEC = 39 mg/kg dry wt. 28d-LC_{50} = 166 mg/kg dry wt.	Test to OECD TG 218, reliability score 1. Endpoints mortality, mean development times, emergence ratios and development rates. Measured concentration. Artificial sediment.	Registration dossier (study report 2009),
Hyallela azteca	28d-NOEC ≥70 mg/kg dry wt. 28d-LC_{50} >70 mg/kg dry wt.	Test to OPPTS Guideline 850.1735, reliability score 1. Endpoints survival and weight. Measured concentration. Natural sediment.	Registration dossier (study report 2009),
Lumbriculus variegatus	28d-NOEC = 1.1 mg/kg dry wt. 28d-EC_{50} >17 mg/kg dry wt.	Test to OECD 225/OPPTS Guideline 850.1735, reliability 1/2. Survival and reproduction. Measured concentration. Artificial sediment.	Registration dossier (study report 2009),
Lumbriculus variegatus	NOEC = 38 mg/kg dw No effects.	Test to OECD 225/OPPTS Guideline 850.1735, reliability 2. Survival and reproduction. Measured concentration. Natural sediment	Registration dossier (study report 2013),
Lumbriculus variegatus	NOEC = 7.8 mg/kg dry wt. No effects	Test to OECD TG 225. Reliability 1. Reproduction and biomass. Measured consentration. Artifical sediment.	Registration dossier (study report 2017),

Toxicity was observed in two of five sediment tests, however the reliability of the test with the lowest NOEC is questioned, as discussed above. Thus, the lowest NOEC of the other four studies is used – 7.8 mg/kg dw giving a NOEC of 18.6 mg/kg dw when normalised to a 5 % organic carbon content.

The data shows no effects at the highest concentrations tested in the studies. A true PNEC cannot be calculated from the test data because the NOEC values that have been determined are limited values.
Based on the five studies the lowest NOEC in the other four studies is used – 7.8 mg/kg dw, giving a NOEC of 18.67 mg/kg dw when normalised to 5% carbon content.

Applying an assessment factor of 10 this gives a of PNECsediment=1.86 mg/kg dw.

7.8.1.5. Other aquatic organisms

None.

7.8.2. Terrestrial compartment

Table 32: Summary of toxicity to soil microorganisms

Species	Value	Remarks	Reference
Soil microorganisms	28d-EC50 >6.5 mg/kg soil dw	OECD TG 216 (Soil Microorganisms: Nitrogen Transformation Test)	Registration dossier (study report 2016),

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 33: Summary of microbiological activity in sewage treatment systems

Species	Value	Remarks	Reference
Activated sewage sludge	EC50 (3 h) > 100 mg/l	OECD TG 209 Read-across from L4	Registration dossier (study report 2010)

The microbiological toxicity data given in the registration dossier are summarised in Table 33. The data relate to the read-across substance L4 (decamethyltetrasiloxane, CAS RN 141-62-8, EC No. 205-491-7). There are no data for L3 itself. L4 is not toxic to activated sewage sludge at concentrations up to 100 mg/l and the Registrant(s) concluded that L3 would behave similarly to L4.
A read-across table summarising the results of 13 microorganism tests is also provided as supporting information in the registration dossier. None of these are reported to exhibit toxicity[19].

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

In principle, the eMSCA is cautious at the direction of read-across in the category being used for this endpoint. This is because L3 would be expected to be more bioavailable than L4, as L3 is more water soluble and of lower log Kow. In this instance, the wider 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 L3.

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

[19] One test performed with D4 using *Escherichia coli* and *Staphylococcus aureus* over 24 h is described as exhibiting “little or no toxicity”

7.8.4. Summary and discussion of the environmental hazard assessment

The available ecotoxicity data show that L3 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 L3 does not fulfil the T-criterion based on ecotoxicity. However, effects in other taxa cannot be excluded.

Toxicity was observed in two of five sediment tests, however the reliability of the test with the lowest NOEC is questioned. Based on the other four sediment tests a PNEC of 1.86 mg/kg dw was derived. However, the NOEC used to derive this PNEC is a limit value thus this PNEC should be used with caution.

7.8.5. PNEC derivation and other hazard conclusions

Table 34: 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.
Marine water		
Intermittent releases to water		
Sediments (freshwater)	Using the Lumbriculus 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	Assessment factor 100
Soil	n/a	The Registrant(s) have not derived any PNEC soil because of the lack of effects in the available test.
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	Assessmentt 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]

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

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.

7.9. Human Health hazard assessment

No specific concerns for human health were listed on the CoRAP. 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/vPvB substances in Annex XIII of REACH; as such, only the end-points carcinogenicity, germ cell mutagenicity, reproductive toxicity and repeated-dose toxicity were evaluated.

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).

7.9.1. Toxicokinetics

Not relevant to the targeted evaluation.

7.9.2. Acute toxicity and Corrosion / Irritation

This information is not relevant to the evaluation.

7.9.3. Sensitisation

This information is not relevant to the evaluation.

7.9.4. Repeated dose toxicity

7.9.4.1. Repeated-dose toxicity: oral

The repeated dose oral toxicity of octamethyltrisiloxane (L3) has been investigated in two oral studies, one non-guideline range-finding study and one 28-day oral study in rats (OECD TG 407).

Table 35: Summary of repeated-dose studies via the oral route

Method	Results	Remarks
7-day repeat dose. (oral, gavage) Rat (Sprague Dawley) 0, 100, 300 or 1000 mg/kg bw/d Vehicle: corn oil 5 per sex/dose Registration dossier 7.5.361 [2010]	**100 mg/kg bw/day** Slight ↓ mean body weight, ↑ mean absolute liver weight (10%) in females, ↑ mean liver-to-body weight ratio (females). None of these differences were statistically significant. **300 mg/kg bw/day** Slight ↓mean body weight (males). Significantly ↑ mean absolute and mean relative liver weight (males); significantly ↑ mean liver-to-body weight ratio (females). Significantly ↑ mean absolute spleen weight and mean spleen-to-body weight ratio (males). Magnitude of these changes not stated in IUCLID dossier. **1000 mg/kg bw/d (above the level of classification)** Slight ↓ mean body weight, significantly ↑ mean absolute liver weights and mean liver-to-body weight ratios (males and females). ↑ mean absolute kidney weight and mean kidney-to-body weight ratio (males). ↑ mean absolute spleen weight of males (+14%) (not statistically significant). Significantly ↑ spleen-to-body weight ratio (males). NOAEL: none set as this was a range-finding study.	Test material octamethyl-trisiloxane (L3) Non guideline range finding study. Reliability: 4 Reliability proposal from Registrant (s). Original study report not consulted by the eMSCA.

Method	Results	Remarks
28-day repeat dose study + 14 day recovery (oral, gavage) Rat (Sprague-Dawley) 0, 5, 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 7.5.512 [2010]	**Control** Dark red foci in the mucosa of the stomach (1 male); unilateral renal pelvis dilation (1 male); red foci or reddish discoloration of the thymus (1male/1 female) **5 mg/kg bw/d** No treatment related effects. **25 mg/kg bw/d** ↑ Liver/body weight ratio (+12% males) statistically significant; dilation of the uterus (1 female); hyaline droplets (minimal to slight severity) (males). ↑ serum potassium (males). **250 mg/kg bw/d** ORGAN WEIGHTS: ↑ absolute liver weights (+56% males (significant)). ↑ liver-to-body weight (+52% males; +12% females) statistically significant, ↑ liver/brain weight ratio (+57% males) statistically significant, ↓ absolute brain weights (-4%, female). GROSS PATHOLOGY: enlargement and dark or black brown discoloration of the liver in all males; dark red nodules in epididymal adipose tissue (1 male), dilation of the uterus (1 female). Clinical chemistry: significantly ↑ total cholesterol (60.7%) and phospholipids (42.2.%) (males) and; significantly ↑ total bilirubin (51.2% males; 54.5% females). HISTOPATHOLOGY – LIVER: Protoporphyrin accumulation in the intra-hepatic bile ducts, Kupffer cells and hepatocytes accompanied by periportal chronic inflammation, bile duct proliferation and centrilobular hepatocellular hypertrophy.	Test material: octamethyl-trisiloxane (L3) Reliability: 1

Dose (ppm)	0		25		250		1000	
	Number of animals (Mean Severity)*							
Terminal sacrifice	M	F	M	F	M	F	M	F
Centrilobular hepatocellular hypertrophy	0 -	0 -	0 -	0 -	2 (1.0)	0 -	3 (1.0)	3 (1.0)
Protoporphyrin accumulation								
Intrahepatic bile ducts	0 -	0 -	0 -	0 -	5 (2.8)	0 -	5 (3.0)	2 (2.0)
Kupffer's cells	0 -	0 -	0 -	0 -	1 (1.0)	0 -	5 (2.0)	0 -
hepatocytes	0 -	0 -	0 -	0 -	3 (1.0)	0 -	5 (1.0)	0 -
Periportal chronic inflammation	0 -	0 -	0 -	0 -	5 (1.2)	0 -	5 (1.0)	2 (1.0)
Bile duct proliferation	0 -	0 -	0 -	0 -	4 (1.8)	0 -	5 (1.8)	1 (1.0)
Recovery group	M	F	M	F	M	F	M	F
Protoporphyrin accumulation								
Intrahepatic bile ducts	-	-					5 (3.0)	4 (1.5)
Kupffer's cells	-	-					5 (1.8)	-
hepatocytes	-	-					5 (1.0)	-
Periportal chronic inflammation	-	-					5 (1.0)	2 (1.0)

Method	Results	Remarks

Bile duct proliferation	-	-		5 (2.0)	-

**Severity grades for clinical symptoms assigned as follows: 0=not present, 1 = present/slight, 2= moderate, 3=marked.*

KIDNEY – Hyaline droplets (minimal to slight in all males); not evident in animals after recovery period. Immunohistochemistry for α-2u globulin (globular staining) showed a similar dose effect.

At 1000 mg/kg/d (above the level for classification)
↓ body weight (males) and body weight gain (intermittent).

Changes in haematology, clinical chemistry and urinalysis. Statistically significant changes in males: increased number of red blood cells, decreased mean corpuscular volume and mean cell hemoglobin

↑ absolute liver weights (+56% males; +37% female) statistically significant, ↑ relative liver weight (+78% and +45%, males and females respectively). ↑ liver/brain weight (+62%/+44% for males/females). ↓ absolute heart weight (males), ↓ pituitary gland weight (males), ↑ mean kidney/body weight (+21%, males), ↓ mean heart/brain weight ratio (significant, males). ↓ absolute brain weights (female).

After two weeks recovery, ↓ body weight (males), ↓ absolute brain weights (males), ↓ combined seminal vesicles/prostate glands weights, ↓ weight of epididymides. ↑ testes/body weight ratio and testes/brain weight ratios. ↓ seminal vesicles and prostate/brain weight). ↑ liver/brain weight ratios (males). ↑ mean liver/body weight ratio(males, females).

Gross pathology: Dark or black brown discoloration of the liver still present in males at the end of recovery. Discoloured lymph nodes (in one male).

Clinical chemistry: ↑ aspartate aminotransferase, alanine aminotransferase and gamma glutamyltransferase (males). ↑ total cholesterol and phospholipid (both sexes); ↑ triglyceride (97%, females). ↑ total bilirubin (41.4%, males). ↑ globulin (both sexes) and ↓ albumin/globulin ratio (males). ↑ Na and Cl (males); ↑ potassium.

HISTOPATHOLOGY – LIVER: Protoporphyrin accumulation in the intra-hepatic bile ducts, Kupffer cells (males) and hepatocytes (males). Periportal chronic inflammation and bile duct proliferation. Hepatocellular hypertrophy. With the exception of hepatocellular hypertrophy in both sexes and bile duct proliferation in females, these findings persisted after the 14 day recovery period.

HISTOPATHOLOGY – KIDNEY: Hyaline droplets (minimal to slight severity) (group 3, 4 and 5; males); not present at the end of the recovery. Immunohistochemistry for α-2u globulin showed a similar dose effect as seen with hyaline droplets.

HISTOPATHOLOGY – THYROID: Follicular cell hypertrophy (minimal severity) (2 males, 1 female; not seen at the end of the recovery period.

NOAEL: 25 mg/kg bw/d <u>for males</u> based on liver findings at 250 mg/kg/d; and 250 mg/kg bw/d <u>in females</u> based on liver weight and morphological changes that were shown not to be reversible at 1000 mg/kg/d.

In a non-guideline range-finding study rats were dosed with L3 over a period of 7 days. No mortality was observed at any of the doses tested. The main target organs were the liver, kidney and spleen. Statistically significant increases in absolute liver and spleen

weights were seen in males at 300 mg/kg bw/d. At the top dose, which is above the guidance value for classification, a statistically significant increase in absolute liver weight was also observed in females. In males treated at the top dose, increases in kidney weight were also reported in addition to the effects on liver and spleen. No dose related effects were reported at 100 mg/kg bw/d.

In a guideline study according to OECD TG 407, rats were dosed with L3 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 adjusted from a 90-day oral study to a 28-day study) the main effect was on the liver. Absolute liver weight increased in a statistically significant manner in males (+56%). The increase in males is considered to be adverse (≥20%) and was associated with liver enlargement, dark brown or black-brown discolouration and protoporphyrin accumulation, periportal chronic inflammation, bile duct proliferation (minimal to slight) and centrilobular hypertrophy (minimal severity). At the top dose, which is above the guidance value for classification, the increases in liver weight in males remained at 56%, while in females the increase became adverse and statistically significant (+37%). Also at the top dose, clinical chemistry showed changes in the serum activity of liver marker enzymes (increase mean activity of aspartate aminotransferase, alanine aminotransferase in males and an increase in cholesterol and phospholipid levels in both sexes), consistent with the other liver changes reported. At the end of the recovery period (top dose group only) increases in the liver to body weight ratio were still present as was the discoloration of the liver, protoporphyrin accumulation, periportal chronic inflammation and bile duct proliferation.

In the kidneys of male rats, a dose related increase in hyaline droplets and alpha-2u globulin were observed. This finding is species-specific and is therefore not considered relevant to human risk assessment.

The NOAELs from this study are 25 mg/kg bw/d for males based on liver findings at 250 mg/kg/d, and 250 mg/kg bw/d in females based on liver weight and morphological changes that were shown not to be reversible at 1000 mg/kg/d.

7.9.4.2. Repeated-dose toxicity: inhalation

Two repeated-dose studies were carried out via the inhalation route: a 90-day repeated-dose study according to OECD TG 413 and a 28-day repeated-dose combined with a reproduction/developmental screening study (OECD TG 422). The results from the combined study that are relevant to reproductive toxicity are described in Section 7.9.7.

Table 36: Summary of repeated-dose studies via the inhalation route

Method	Results	Remarks
90-day repeated dose study + 28 day recovery (inhalation (vapour) 6 hours daily whole body) Rat (Sprague-Dawley) 0, 95, 400 and 3200 ppm (nominal) equivalent to approx. 0.9, 3.9 and 31 mg/l/6h/d or internal doses* of 243, 1053 and 8370 mg/kg bw/d	**Control** Periportal chronic inflammation (1 male and 1 female; severity 1) **95 ppm (0.9 mg/l/6h/d or an internal dose of 243 mg/kg bw/d)** Periportal chronic inflammation (1 female); bile duct proliferation (1 female); minimal to slight hyaline droplets was noted in the kidneys (1 male). **At doses above the guideline value for classification:** **400 ppm (3.9 mg/l/6h/d or an internal dose of 1053 mg/kg bw/d)** ↑ cholesterol levels (+8% females); ↑ total protein and globulin (4.4% and 10.1% females), ↑ absolute liver weights (11.1% males), ↑ relative liver weights (12.1% (males)). Centrilobular hepatocellular hypertrophy minimal to slight severity 4 males), periportal chronic inflammation (1 male and 1 female) and bile duct proliferation (1 female). Minimal to slight hyaline droplets (3 males).	Test material: octamethyl trisiloxane (L3) Reliability: 1

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 7.5.508 [Ref 2011]

3200 ppm (31 mg/l/6h/d or a calculated internal dose of 8370 mg/kg bw/d)
↑ cholesterol levels (not apparent at the end of the recovery period); ↑ total protein and globulin values (males: +6.4% for protein and + 13.8% for globulin; females: +5.4% for protein and +14.7% for globulin), statistically significant ↑ absolute liver weights 22.1% (males) and 26.5% (females), statistically significant ↑ relative liver weights 24.6% (males) and 26.6% (females). This was still apparent but less marked at the end of the recovery period in males. Centrilobular hepatocellular hypertrophy (minimal to slight severity 9 males and 9 females). Protoporphyrin accumulation (minimal to moderate in all males), periportal chronic inflammation (minimal to slight 10 males/1 female) and bile duct proliferation (9 males).

Dose (ppm)	0		95		400		3200	
	Number of animals (Severity)							
	M	F	M	F	M	F	M	F
Centrilobular hypertrophy	0 (-)	0 (-)	0 (-)	0 (-)	4 (1.0)	0	9 (1.1)	9 (1.2)
Protoporphyrin crystals	0 (-)	0 (-)	0 (-)	0 (-)	0 (-)	0 (-)	10 (2.2)	0 (-)
Periportal chronic inflammation	1 (1.0)	1 (1.0)	0 (-)	1 (1.0)	1 (1.0)	1 (1.0)	10 (1.9)	1 (1.0)
Bile duct proliferation	0 (-)	0 (-)	0 (-)	1 (1.0)	0 (-)	1 (1.0)	9 (1.3)	0 (-)

At end of recovery: protoporphyrin accumulation, periportal chronic inflammation, bile duct proliferation.

Dose (ppm)	0		3200 ppm	
	Number of animals (Severity)			
	M	F	M	F
Centrilobular hypertrophy	0 (-)	0 (-)	2 (1.0)	0 (-)
Protoporphyrin crystals	0 (-)	0 (-)	7 (1.6)	(0) -
Periportal chronic inflammation	4 (1.3)	0 (-)	9 (1.0)	2 (1.5)
Bile duct proliferation	0 (-)	0 (-)	8 (1.0)	2 (1.5)

Proximal tubular hypertrophy in the kidney (minimal to slight) in 9 males and 10 females; hyaline droplets (minimal to slight) in all males; not observed at the end of recovery.

Dose-related increase in α-2u-globulin (males) at all doses (only significant in top dose) with incomplete recovery in top dose group.

NOAEC: 400 ppm (equivalent to 3.9 mg/l/6h/d or an estimated internal dose of 1000 mg/kg bw/d assuming 100% absorption) based on accumulation of protoporphyrin pigments and associated periportal chronic inflammation and bile duct proliferation at the top concentration.

Combined repeated dose toxicity study with reproduction/ developmental screening (inhalation (vapour); 6 hours/day, whole body)

Toxicity phase

All doses tested are above the guideline value for classification. Effects seen in the toxicity phase animals were:

ORGAN WEIGHT: ↑ mean liver weight (15.3%, 19.7% and 26.5% (females), non-statistically significant increase in males); ↑ relative liver weight (4,3%, 2.5% and 15.6% (males) and 12.3%, 19.7% and 23.3% (females). These were statistically significant at all dose levels in females.

CLINICAL CHEMISTRY: ↑ serum cholesterol (statistically significant 1623 ppm and 3146 ppm in females, statistically significantly in all exposed

Test material: octamethyl trisiloxane (L3)
Reliability: 1

Rat (Sprague-Dawley) male/female 806, 1623, and 3146 ppm (equivalent to approximately 8, 16 and 31 mg/l/6h/d or an internal dose* of 2106, 4320 and 8370 mg/kg bw/d) 10/sex/dose for 2 weeks of pre-mating, 2 weeks of mating and through mating (up to 14 days) Males treated for 29 days Females, toxicity phase: 28 days Guideline value for classification for STOT-RE Cat 1 ≤0.6 mg/l/6h/d and Cat 2 ≤3 mg/l/6h/d Reproductive phase: up to and including day 19 gestation. Dams not treated during lactation. OECD TG 422 Registration dossier 7.5.399 [2008]	groups in males) and ↑ serum calcium (females, 3146 ppm). ↓ bilirubin and serum chloride (females, 3146 ppm). All changes were within historical control range. HAEMATOLOGY: ↑ platelet numbers (males, 3146 ppm). HISTOPATHOLOGY – LIVER: centrilobular hypertrophy (corresponding with liver weight increases). Protoporphyrin accumulation accompanied by bile duct proliferation and chronic inflammation.	

Dose	**800 ppm**		**1600 ppm**		**3200 ppm**	
	Males	**Females**	**Males**	**Females**	**Males**	**Females**
Centrilobular hypertrophy						
Minimal	-	6/10	-	3/10	10/10	-
Mild	-	-	-	7/10	-	9/10
Moderate	-	-	-	-	-	1/10
Marked	-	-	-	-	-	-
Porphyria						
Minimal	-	-	1/10	-		-
Mild	-	-	2/10	-	2/10	-
Moderate	-	-	3/10	-	6/10	-
Marked	-	-		-	1/10	-
Bile duct proliferation						
Minimal	-	-	1/10	-	-	-
Mild	-	-	2/10	-	2/10	-
Moderate	-	-	3/10	-	6/10	-
Marked	-	-	-	-	1/10-	-
Chronic inflammation						
Minimal	-	-	1/10	-	2/10	-
Mild	-	-	2/10	-	6/10	-
Moderate	-	-	3/10	-	1/10	-
Marked	-	-	-	-		-

- Not seen (0/10 animals)

HISTOPATHOLOGY – KIDNEY: microscopic changes showed protein droplet nephropathy (males, all doses, becoming more common at higher doses) along with individual cell necrosis and tubular basophilia and granular casts (consistent with α-2u-globulin nephropathy).

Thyroid: ↑ follicular hypertrophy (minimal to mild, males and females, 3146 ppm).

NOAEC: >3146 ppm (31 mg/l/6 h/d or an estimated internal dose of 8370 mg/kg bw/d assuming 100% absorption), for females. No NOAEC is proposed for males; the LOAEC is 806 ppm (8 mg/l/6h/d) based on protein droplet nephropathy at the lowest concentration and hepatic protoporphyrinosis at the mid- and top-concentrations (≥16 mg/l/6h/d).

Fertility and Development
Results from the reproductive and developmental phases of the study are reported at Section 7.9.7.

* 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 guideline study according to OECD TG 413, rats were exposed to L3 via the inhalation route for 90 days. No mortality was observed at any of the doses tested. At 0.9 mg/l/6h/d, a dose that is only marginally below the guidance value for classification for STOT-RE of ≤1 mg/l/6h/d, the only effects observed was periportal chronic inflammation and bile duct proliferation, both in one female and slight proximal tubular hypertrophy observed in the kidney of one male. At doses above the guideline for classification, increases in liver weight, together with changes in histopathology and changes in clinical chemistry (consistent with liver effects) were observed. Effects in the kidneys at doses above the guidance value for classification were only observed in male rats and were confined to proximal tubular hypertrophy of minimal to slight degree, hyaline droplets and alpha-2u globulin.

A NOAEC of 400 ppm (equivalent to 3.9 mg/l/6h/d or an estimated internal dose of 1000 mg/kg bw/d assuming 100% absorption) is proposed based on accumulation of protoporphyrin pigments and associated periportal chronic inflammation and bile duct proliferation at the top concentration.

In a second inhalation study incorporating a reproductive/developmental screening, all the doses tested were above the guideline values for classification for repeated-dose toxicity. Reported effects were consistent with the previous findings and included increased liver weight with centrilobular hypertrophy, porphyria, bile duct proliferation and inflammation, microscopic effects on the kidney and follicular hypertrophy of the thyroid. Effects relevant to reproductive toxicity are considered under Section 7.9.7.

A NOAEC of >3146 ppm (31 mg/l/6 h/d or an estimated internal dose of 8370 mg/kg bw/d assuming 100% absorption), the highest concentration tested, is proposed for females. No NOAEC is proposed for males; the LOAEC is 806 ppm (8 mg/l/6h/d) based on protein droplet nephropathy at the lowest concentration and hepatic protoporphyrinosis at the mid- and top-concentrations (≥16 mg/l/6h/d).

7.9.4.3. Summary of Repeated-Dose Toxicity

The short-term toxicity of L3 was investigated via the oral and inhalation routes in rats. The main findings were on the liver and kidney.

Liver

Effects on the liver were observed following treatment via both oral and inhalation routes. Increased liver weight, considered to be adverse in males, was reported in males and females at doses below/at the guidance value for classification in the 7 and 28 day oral studies. This was accompanied by enlargement and discolouration, protoporphyrin accumulation, periportal chronic inflammation, bile duct proliferation and centrilobular hypertrophy. Changes in clinical chemistry, indicative of liver toxicity, were reported at doses below the (adjusted) guidance values for classification. In the studies via the inhalation route, effects on the liver were confined to concentrations far in excess of the guidance value for classification. Furthermore, an increase in the duration of the study did not result in a marked difference in the severity or incidence of the reported effects.

Kidney

Effects on the kidney in male rats at dose levels below the guidance values were confined to hyaline droplet formation in animals dosed with 25 and 250 mg/kg bw/d and alpha-2u globulin deposition in male animals dosed at 250 mg/kg bw/d. The hyaline-droplet formation was recorded as minimal to slight. Hyaline droplet formation is species-specific and is therefore not considered relevant to human hazard characterisation. No other effects on the kidney were observed at levels below the guidance values for classification.

A classification for STOT-RE is indicated when toxic effects that may include the following descriptions occur at or below 300 mg/kg/d in a 28-day oral rat study or ≤1 mg/l in a 90-day inhalation study or ≤3 mg/l in a 28 day inhalation 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 dose/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 in haematology and urinalysis at doses below the guidance values. Changes in clinical biochemistry were observed at doses below the guidance values for classification and while not considered adverse in isolation are consistent with liver dysfunction.

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 (eg. severe fatty change in the liver)
In the 28-day repeated-dose oral study all animals showed increases in liver weight at doses below the guideline for classification. The liver-weight increase was considered adverse in males at doses of 250 and 1000 mg/kg bw/d while in females the increase was only found to be adverse at the top dose (above the guideline for classification). No information is available on the impact of liver weight increase of the magnitude reported on other organs. In addition to increased liver weight, enlargement and discolouration of the liver was noted in males at corresponding dose levels. Microscopically, protoporphyrin accumulation was observed in the intrahepatic bile duct, Kupffer cells and hepatocytes of males at minimal to moderate severity, as was periportal chronic inflammation and bile duct proliferation at 250 mg/kg/d and above. In the recovery group animals (dosed at levels exceeding the guideline for classification), the microscopic findings were still present at the end of the recovery period. No microscopic effects were noted in the females at doses below the guideline for classification. The finding of protoporphyrin accumulation is considered relevant to the human risk assessment as it is indicative of a potential to cause porphyria in humans. The liver weight increase, protoporphyrin accumulation and periportal chronic inflammation are therefore considered to be relevant to classification for STOT-RE. No other morphological findings were reported in the liver at doses below the guideline for classification in animals dosed via the oral route.

No adverse effects on the liver were reported at levels below the guideline levels for classification in either of the studies in which animals were exposed by the inhalation route for 28- and 90-days and although liver findings consistent with those reported following oral dosing were seen, these were at concentrations well in excess of the guidance values for classification. A simple conversion to systemic doses indicates that the liver findings from the inhalation studies were only seen at doses well above the equivalent oral classification level. However, this difference in effect level may be due to a first pass effect.

In the kidney, the key finding was hyaline droplet formation and α-2u globulin formation. This finding is species-specific and is not considered relevant for human hazard characterisation.

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, the liver is a clear target organ. Adverse increases in liver weight (≥20%) were observed in males at 250 mg/kg bw/d, which in the 28-day repeated-dose oral study was associated with changes in gross pathology, histopathology and clinical chemistry that are consistent with liver toxicity. The dose of 250 mg/kg bw/d is below the adjusted guideline value for classification as STOT-RE2. At this dose level, the liver effects observed in females were not considered adverse.

At higher doses, the effect on liver weight was considered adverse (≥20%) and was associated with observations on clinical chemistry and histopathology that are evidence of liver dysfunction. While the changes observed at 1000 mg/kg bw/d in females are above the guideline value for classification, they show that there is a progression in the severity of effects with increasing dose. These results are based on findings in a small number of animals. There is thus no longer term (90-day) oral study, which utilises larger study groups available to confirm the results.

Similar findings are reported for the related substances L4 and L5, however the effects reported are less severe. Given the longer chain lengths of L4 and L5, and higher molecular weight, it might be anticipated that they are of lower toxicity on a mg/kg bw basis and therefore this finding is not unexpected.

A 28-day repeated dose study with L2 is also available, which being of shorter chain length might be expected to be more toxic than L3. The eMSCA does not consider that the L2 study provides any additional information of use in concluding on the repeated-dose toxicity of L3 due to the dose spacing used in the study. Effects of similar magnitude were seen in the study with L2 at the much higher dose of 640 mg/kg bw/d (compared to 250 mg/kg bw/d in the L3 study) while they were not seen at doses of L2 of 160 mg/kg bw/d (well below the level that caused these effects with L3). The only longer duration studies with L3 are via the inhalation route.

In the 90-day repeated dose inhalation study, the only liver findings seen at doses below the guideline for classification in treated animals were periportal chronic inflammation and bile duct proliferation, which occurred at levels comparable to those seen in control animals. Only at much higher doses were the changes in liver weight considered adverse (over 20%). Although this increase was only marginally over 20% it was accompanied by a higher incidence and severity of centrilobular hypertrophy, protoporphyrin accumulation periportal chronic inflammation and bile duct inflammation. No changes in clinical chemistry indicative of liver toxicity were seen. This difference may be a consequence of the route of dosing with the liver being exposed to a high dose over a short space of time, while exposure from inhalation is over 6 hours and results in distribution of the test material throughout the body rather than directly to the liver.

While the calculated internal doses following inhalation exposure appear considerably higher than those from oral dosing, there is a high degree of uncertainty surrounding these values given the absence of absorption data from treatment via the oral and inhalation routes. Given this, direct comparison of effects from oral and inhalation exposure is not possible.

The studies indicate adverse liver weight increases of >50% in males at dose levels below the guideline for classification, accompanied by liver enlargement, changes in histopathology and altered clinical chemistry consistent with liver toxicity. In particular the observation of protoporphyrin accumulation is considered relevant to the human risk assessment as it is indicative of a potential to cause porphyria in humans. Furthermore, an increase in liver weight of the magnitude reported has the potential to impact on other organs systems, although no further information is available on this aspect.

Even if these effects are observed below the guidance values for classification, are dose-related (observed in some males), and are somewhat irreversible, they are probably not sufficiently severe. In addition, they are not observed by inhalation and there are no 90-day study by the oral route.

The data are borderline and the eMSCA does not propose a harmonised classification as STOT RE2; H373 (May cause damage to organs (liver) through prolonged or repeated (oral) exposure).

7.9.5. Mutagenicity

The genotoxicity of L3 was investigated in a Bacterial reverse mutation assay and an *in vitro* mammalian chromosome aberration test. The results of the genotoxicity testing are summarised in Table 37.

7.9.5.1. In vitro genotoxicity data

Table 37: 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 7.6.1.1.342 [2008]	Negative both in the presence and absence of metabolic activation. No cytotoxicity was reported at concentrations up to the limit dose.	Test Material: octamethyl-trisiloxane (L3) Reliability: 1
In vitro mammalian chromosome aberration test Chinese Hamster Ovary (CHO) cells OECD TG 473 Test concentrations: Without metabolic activation: 2.5, 5, 12.5 µg/ml (4 hour exposure); 5, 10, 15 µg/ml (20 hour exposure); With metabolic activation: 10, 25 and 75 µg/ml (4 hours exposure). Appropriate positive controls and solvent controls. Registration dossier 7.6.1.2.106 [2008]	Test reported as negative both in the presence and absence of metabolic activation. Substantial cytotoxicity observed at dose levels > 23.4 µg/ml in all treatment groups	Test material: octamethyl-trisiloxane (L3) Reliability: 1

L3 has been tested in an Ames test and an *in vitro* mammalian chromosome aberration test. Both were performed according to the OECD guidelines and GLP. The results of both tests were negative in both the presence and absence of metabolic activation.

No further data is necessary to conclude on this endpoint, however two further *in vitro* mammalian cell gene mutation assays performed with closely related substances hexamethyldisiloxane (L2) and decamethyltetrasiloxane (L4) were included in the registration dossier. Both studies gave negative results which support the findings from the studies with L3.

Overall, the *in vitro* data are negative.

7.9.5.2. In vivo genotoxicity data

Based on the negative results from the *in vitro testing*, the requirement for testing *in vivo* is not triggered.

7.9.5.3. Human information

No information available.

7.9.5.4. Summary and discussion of mutagenicity

Two *in vitro* studies performed with L3 were submitted as part of the registration dossier. L3 tested negative in both the bacterial reverse mutation assay and the mammalian chromosome aberration test. Based on the results of the tests carried out with L3, testing *in vivo* is not necessary.

Overall L3 is considered not to be mutagenic.

7.9.6. Carcinogenicity

No chronic repeat-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.* The data raise no concerns for the carcinogenic potential of L3.

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 TG 422). Results for the reproductive group are reported in Table 38 below. Results from the toxicity group are reported under Section 7.9.4.2.

Table 38: Summary of reproductive effects from the combined repeated-dose study with reproductive/developmental screening and prenatal developmental toxicity study

Method	Results	Remarks
Combined repeated dose toxicity study with reproduction/developmental screening (inhalation; 6 hours/day, whole body) Rat (Sprague-Dawley) male/female 806, 1623, and 3146 ppm (equivalent to approximately 8, 16 and 31 mg/l/6h/d or internal doses* of 2106, 4320 and 8370 mg/kg bw/d) 10/sex/dose for 2 weeks of pre-mating, 2 weeks of mating and through mating (up to 14 days) Males treated for 29 days Females Toxicity phase: 28 days Reproductive phase: up to and including day 19 gestation. Dams not treated during lactation. OECD TG 422 Registration dossier 7.5.399 [2008]	See Section 7.9.4.2 (table) for results from toxicity phase. **Parental:** **At 806 ppm:** One animal failed to mate. A second showed no evidence of mating, but had 15 pups *in utero* on necropsy. **Fertility** No effects on weight of testes, seminal vesicle, epididymides or prostate, duration of gestation, number of implantation sites, mean number of corpora lutea, number of implantations or total number of pups. **Developmental (Offspring):** No effects on sex ratio, pup viability, pup body weight or litter weight. One pup in low concentration group was born without a tail or penile and anal opening. NOAEL (fertility): 3146 ppm (equivalent to approximately 31 mg/l/6h/d or 8370 mg/kg bw/d) NOAEL (developmental): 3146 ppm (equivalent to approximately 31 mg/l/6h/d or 8370 mg/kg bw/d)	Test material: octamethyl-trisiloxane (L3) Reliability: 1
Developmental toxicity study According to OECD TG 414 (Prenatal Developmental Toxicity Study) and EPA OPPTS 870.3700	**Maternal animals:** There were treatment-related, statistically significant increases in mean absolute and relative liver weights at all dose levels tested with correlating histopathological observations. The mean relative liver weights of females	Test material: octamethyl-trisiloxane (L3) Reliability: 1

Method	Results	Remarks
Rat (Crj: CD(SD)) time-mated females, 24 per dose oral: gavage: 0, 75, 250 and 750 mg/kg bw/day Vehicle: corn oil – (dried and deacidified corn oil) Exposure: GD 6-20 (Daily) [2017]	given 75, 250, or 750 mg/kg/day were 9.3%, 13.5%, or 29.5% higher than controls, respectively. Treatment-related very slight hypertrophy of centrilobular/midzonal hepatocytes was present in 12/24 females given 75 mg/kg/day and in 17/24 females given 250 mg/kg/day. Treatment-related slight hypertrophy of centrilobular/midzonal hepatocytes was present in 7/24 females given 250 mg/kg/day and in 24/24 females given 750 mg/kg/day. The hepatocellular hypertrophy corresponded to the dose related increases in liver weights of females given 75, 250 or 750 mg/kg/day. Two females given 750 mg/kg/day had treatment-related very slight multifocal chronic inflammation in periportal regions of the liver, and one of the females with chronic inflammation also had treatment-related very slight increased number of mitotic figures in hepatocytes. Treatment-related pigment deposits were present in the intrahepatic bile ducts, hepatocytes and/or Kupffer cells of six females given 750 mg/kg/day. The pigment deposits were brown when examined with a light microscope and birefringent with some deposits featuring Maltese cross formations when examined with polarized light. All of the treatment-related liver effects were consistent with a previously conducted 28-day oral gavage toxicity study with octamethyltrisiloxane described above. Maternal reproductive toxicity: no effects observed NOAEL: 250 mg/kg bw/day based on: Based on the liver weight increases combined with the chronic inflammation of the liver noted in animals in the 750 mg/kg/day group. **Fetuses:** There was no indication of embryo/fetal toxicity or teratogenicity at any dose level tested. NOEL: 750 mg/kg bw/day 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

No effects on male or female reproductive parameters were observed in the study. The weights of testes, seminal vesicle, epididymides and prostate were similarly unaffected. Duration of gestation, number of implantations and corpora lutea and the total number of live pups were comparable to control animals.

7.9.7.2. Effects on offspring

One pup was born without a tail or penile and anal openings in the low concentration group. This finding is considered incidental and unrelated to treatment as there were no effects reported at higher concentrations. There were no effects on the sex ratio, pup viability, pup body or litter weight.

7.9.7.3. Summary of reproductive toxicity

The reproductive toxicity of octamethyltrisiloxane (L3) was investigated in a combined repeated-dose toxicity study with the reproduction/developmental toxicity screening (OECD 422). There were no effects reported on either fertility or developmental parameters up to the highest concentration tested of 3146 ppm (equivalent to approximately 31 mg/l/6h/d or an internal dose of 8370 mg/kg bw/d). In addition, the lack of significant effects on the reproductive organs in both the 28-day oral and the 90-day inhalation studies support the conclusion that exposure to octamethyltrisiloxane does not affect fertility.

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 /vPvB substances in Annex XIII of REACH; 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 and sensitisation) were not evaluated.

There is no information available on the effects of repeated exposure to L3 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. Effects on the liver identified in the 28-day oral study were increased liver weight, with associated changes in gross pathology, clinical chemistry and histopathology. The dose levels at which these findings were observed are consistent with the criteria for classification as STOT-RE2. Similar effects were reported following exposure via the inhalation route, but at concentrations that were far in excess of the guidance cut-off values for classification. L3 does not meet the criteria for classification via the inhalation route.

The mutagenic potential of L3 has been investigated *in vitro* in bacteria in the Ames test, and in mammalian cells in a bone marrow chromosome aberration test in which it tested negative. The available data do not raise any concerns for the mutagenic potential of L3.

There is no information on the carcinogenic potential of L3, however the results from the *in vitro* genotoxicity testing were negative. Therefore, no specific concerns for carcinogenicity are raised.

The reproductive toxicity of L3 has been investigated in animals in a combined repeated-dose toxicity study with reproductive/developmental toxicity screen (OECD 422). There were no effects reported on either fertility or 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 or reproductive toxicity.

Table 39: 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 (females)	250 mg/kg bw/d (males) 1000 mg/kg bw/d	Liver findings Lack of reversibility of liver effects.
Rat, 90 day inhalation		400 ppm (equivalent to 3.9 mg/l/6h/d)	3200 ppm (equivalent to 31 mg/l/6h/d)	Accumulation of protoporphyrin pigment, periportal chronic inflammation and bile duct proliferation
Rat, combined toxicity with reproductive/ developmental screening	Systemic	>3146 ppm (31 mg/l) (females)	-	No treatment-related effects at highest concentration tested. Effects in males not relevant for human risk assessment.
	Maternal	>3146 ppm (31 mg/l)	-	No treatment-related effects at highest concentration tested
	Fertility	>3146 ppm (31 mg/l)	-	No treatment-related effects at highest concentration tested
	Developmental	>3146 ppm (31 mg/l)	-	No treatment-related effects at highest concentration tested

7.10. Assessment of endocrine disrupting (ED) properties

Not assessed.

7.11. PBT and vPvB assessment

Persistence

Experimental data show a hydrolysis half-life of 13.7 days at pH 7 and 25 °C. The half-life for hydrolysis is however 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 52 days can be obtained.

L3 is not readily biodegradable (0% in 28 days) in a screening test on ready biodegradability (OECD 310) and the screening criteria for P and vP of REACH Annex XIII is met. A reliable sediment simulation study (OECD TG 308) is available on the potential for degradation of L3 in sediments. The study demonstrates a long degradation half-life of 3.5 – 6.9 years in sediment at 12° C. L3 thereby fulfils the P and vP criteria of REACH Annex XIII.

Overall, the available experimental data for L3 demonstrates that the substance fulfils the persistent (P) and very persistent (vP) criteria of REACH Annex XIII.

Bioaccumulation

L3 has a log Kow of 6.6 and therefore meets the screening criteria for B and vB of REACH Annex XIII. The BCF in fathead minnow (*Pimephales promelas)*, has been determined to be in the range 9,500 to 20,342 l/kg, when normalised to a 5% lipid content, and the non-lipid normalised value is up to 7,730 l/kg, meeting the criteria for bioaccumulative (B) and very bioaccumulative (vB) of REACH Annex XIII.
Supporting evidence is provided by the results of a dietary accumulation study with rainbow trout (*Oncorhynchus mykiss)*. This study shows that the growth-corrected and lipid normalised kinetic BMF for L3 is around 0.38 to 0.45. Although BMF are below 1, eMSCA does not consider that a BMF from a fish feeding study is equivalent to a field BMF. This is because, the only contaminant exposure is via food, and the test is performed in clean water, potentially allowing greater depuration to the media during uptake. This means that

a dietary BMF close to, but below 1 can still indicate equivalence to a BCF of above 2000 or 5000 L/kg.

Overall, the aquatic BCF values for L3 significantly exceed the criteria for both bioaccumulative (B) and very bioaccumulative (vB) of REACH Annex XIII.

Toxicity

T criterion based on human health data

The eMSCA assesses the human health data as borderline for STOT RE 2 (target organ: liver) and do not propose a harmonised classification for this health hazard. Based on the available toxicity data, L3 is not considered to fulfil the T-criterion based on human health data.

T criterion based on ecotoxicity data

The available ecotoxicity data show that L3 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 L3 does not fulfil the T-criterion based on ecotoxicity

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

Based on the available data for 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 met, as the human health data indicating a classification of STOT RE 2 due to liver toxicity is borderline. The eMSCA considers the data on environmental hazard as not sufficient for a harmonised classification.

7.12. Exposure assessment

Octamethyltrisiloxane 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 the Registrant(s) had used the approach from the UK Risk Assessment of D5 (Environment Agency, 2009) to determine the releases to air and water for the environmental modelling. The 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 for 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 recently 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 L3, 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. (2013) study is 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 used in the L3 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 have not been conducted. The eMSCA concludes that L3 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

Using the new freshwater sediment PNEC derived by the eMSCA (1.86 mg/kg dwt mg/kg dw), causes the RCR to exceed one (RCR > 1) for several exposure scenarios of L3. This suggests that there are potentially risks from several 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 L3 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.

8. References

ARP, H. 2012. Compilation of Norwegian screening data for selected contaminants (2002-2012). *Miljødirektorat rapport TA,* 2982**,** 571.

BLETSOU, A. A., ASIMAKOPOULOS, A. G., STASINAKIS, A. S., THOMAIDIS, N. S. & KANNAN, K. 2013. Mass loading and fate of linear and cyclic siloxanes in a wastewater treatment plant in Greece. *Environmental science & technology,* 47**,** 1824-1832.

BLYTT, L. D., BRUSKELAND, A. B. & STANG, P. 2013. Organiske miljøgifter i norsk avløpsslam - Resultater fra undersøkelsen i 2012/2013. *In:* BA, N. V. (ed.).

BLYTT, L. D. & STANG, P. 2018. Organic pollutants in Norwegian wastewater sludge – Results from the survey in 2017/18. *In:* BA), N. W. B. N. V. (ed.).

BROOKE, D. & CROOKES, M. 2012. Depuration rate constant: Growth correction and use as an indicator of bioaccumulation potential. *Report LIT,* 7371.

BROOKE, D., CROOKES, M., GRAY, D. & ROBERTSON, S. 2009. Risk Assessment Report: Decamethylcyclopentasiloxane. *In:* BRITAIN, E. A. O. G. (ed.). http://www.environment-agency.gov.uk/: Environment Agency, .

BURKHARD, L. P., ARNOT, J. A., EMBRY, M. R., FARLEY, K. J., HOKE, R. A., KITANO, M., LESLIE, H. A., LOTUFO, G. R., PARKERTON, T. F. & SAPPINGTON, K. G. 2012. Comparing laboratory and field measured bioaccumulation endpoints. *Integrated environmental assessment and management,* 8**,** 17-31.

ECHA 2015. Member State Committee (MSC), Opinion on persistency and bioaccumulation of Octamethylcyclotetrasiloxane (D4) EC Number: 209-136-7 CAS Number: 556-67-2 And Decamethylcyclopentasiloxane (D5) EC Number: 208-764-9 CAS Number: 541-02-6 according to a MSC mandate. Adopted on 22 April 2015. *In:* AGENCY, E. C. (ed.).

ECHA 2016. Background Document to the Opinion on the Annex XV dossier proposing restrictions on Octamethylcyclotetrasiloxane (D4) and Decamethylcyclopentasiloxane (D5)

ECHA (2017). Guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment.

ECHA (2018a). Member State Committee (MSC) Opinion on persistency and bioaccumulation of Octamethylcyclotetrasiloxane (D4) EC Number: 209-136-7 CAS Number: 556-67-2 and Decamethylcyclopentasiloxane (D5) EC Number: 208-764-9 CAS Number: 541-02-6 according to a MSC mandate Adopted on 22 April 2015

ECHA (2018b): Member State Committee, Support document for identification of decamethylcyclopentasiloxane (D5) as a substance of very high concern because of its PBT and vPvB properties (article 57d&e)

ECHA 2020: Background Document to the Opinion on the Annex XV dossier proposing restrictions on Octamethylcyclotetrasiloxane (D4); Decamethylcyclopentasiloxane (D5) and Dodecamethylcyclohexasiloxane (D6)

EVENSET, A., LEKNES, H., CHRISTENSEN, G. N., WARNER, N., REMBERGER, M. & GABRIELSEN, G. W. 2009. Screening of new contaminants in samples from the Norwegian Arctic: Silver, Platinum, Sucralose, Bisphenol A, Tetrabrombisphenol A, Siloxanes, Phtalates (DEHP), Phosphororganic flame retardants.

FOCUS 2014. Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. Version 1.1. FOCUS.

FOCUS, E. 2006. Guidance document on estimating persistence and degradation kinetics from environmental fate studies on pesticides in EU registration.

GOSS, K. U., BROWN, T. N. & ENDO, S. 2013. Elimination half-life as a metric for the bioaccumulation potential of chemicals in aquatic and terrestrial food chains. *Environmental toxicology and chemistry,* 32**,** 1663-1671.

GREEN, N., SCHLABACH, M., STRAND, A., SCHØYEN, M., KAJ, L. 2007. Siloxanes in the environment of the Inner Oslofjord. Report 986/2007. TA2269. Norwegian Pollution Control Authority (SFT).

KAJ, L., ANDERSSON, J., COUSINS, A., REMBERGER, M., EKHEDEN, Y., DUSAN, B., BRORSTRÖM-LUND, E. & CATO, I. 2005a. Results from the Swedish national screening program 2004. Subreport 4: Siloxanes. IVL Report B1643. IVL Swedish Environmental Research Institute, Stockholm.

KAJ, L., SCHLABACH, M., ANDERSSON, J., COUSINS, A. P., SCHMIDBAUER, N. & BRORSTRÖM-LUNDÉN, E. 2005b. Siloxanes in the Nordic environment. *Nordic council of ministers, Copenhagen,* 93.

LEE, S., MOON, H.-B., SONG, G.-J., RA, K., LEE, W.-C. & KANNAN, K. 2014. A nationwide survey and emission estimates of cyclic and linear siloxanes through sludge from wastewater treatment plants in Korea. *Science of the total environment,* 497**,** 106-112.

LIU, N., SHI, Y., LI, W., XU, L. & CAI, Y. 2014. Concentrations and distribution of synthetic musks and siloxanes in sewage sludge of wastewater treatment plants in China. *Science of the Total Environment,* 476**,** 65-72.

MACKAY, D., GOBAS, F., SOLOMON, K., MACLEOD, M., MCLACHLAN, M., POWELL, D. E. & XU, S. 2015. Comment on “Unexpected Occurrence of Volatile Dimethylsiloxanes in Antarctic Soils, Vegetation, Phytoplankton, and Krill”. *Environmental Science & Technology,* 49**,** 7507-7509.

MCGOLDRICK, D. J., LETCHER, R. J., BARRESI, E., KEIR, M. J., SMALL, J., CLARK, M. G., SVERKO, E. & BACKUS, S. M. 2014. Organophosphate flame retardants and organosiloxanes in predatory freshwater fish from locations across Canada. *Environmental Pollution,* 193**,** 254-261.

MONTEMAYOR, B. P., PRICE, B. B. & VAN EGMOND, R. A. 2013. Accounting for intended use application in characterizing the contributions of cyclopentasiloxane (D5) to aquatic loadings following personal care product use: Antiperspirants, skin care products and hair care products. *Chemosphere,* 93**,** 735-740.

OLOFSSON, U., BIGNERT, A. & HAGLUND, P. 2012. Time-trends of metals and organic contaminants in sewage sludge. *Water research,* 46**,** 4841-4851.

PELLETIERA M, ISABEL L, ARMELLIN A, MCDANIELC T, MARTIN P,MCGOLDRICK D, CLARK M AND MOORE S . 2021. Influence of Wastewater Effluents on the Bioaccumulation of Volatile Methylsiloxanes in the St. Lawrence River. Science of the Total Environment

RATOLA, N., SILVA, J., HOMEM, V., SANTOS, L. S., ALVES, A., CINCINELLI, A. & JIMÉNEZ-GUERRERO, P. SILOQUEST-Trying to understand the life of siloxanes in the environment. 9th annual conference of the network on persistent organic pollutants, 2015.

SANCHÍS J, MARTÍNEZ E, GINEBREDA A, FARRÉ M, BARCELÓ D . 2013. Occurrence of linear and cyclic volatile methylsiloxanes in wastewater, surface water and sediments from Catalonia. Science of the Total Environment 443 (2013) 530–538

SANCHÍS, J., CABRERIZO, A., GALBÁN-MALAGÓN, C., BARCELÓ, D., FARRÉ, M. & DACHS, J. 2015a. Response to comments on “Unexpected occurrence of volatile dimethylsiloxanes in Antarctic soils, vegetation, phytoplankton and krill”. *Environmental science & technology,* 49**,** 7510-7512.

SANCHÍS, J., CABRERIZO, A., GALBÁN-MALAGÓN, C., BARCELÓ, D., FARRÉ, M. & DACHS, J. 2015b. Unexpected occurrence of volatile dimethylsiloxanes in Antarctic soils, vegetation, phytoplankton, and krill. *Environmental science & technology,* 49**,** 4415-4424.

SCHLABACH, M, HALSE, AK, KRINGSTAD, A, NIKIFOROV, V, BOHLIN-NIZZETTO, P, PFAFFHUBER, KA, REID, MJ, ROSTKOWSKI, P AND VOGELSANG, C. 2019. Screening program 2018. Volatiles, Gd, BADGE, UV filters, Additives, and Medicines. NILU report.

SCHLABACH, M, VAN BAVEL, B, BAZ-LOMBA, JA, BORGEN, A, FJELD, E, HALSE, AK, NIKIFOROV, V, NIZZETTO, PB, REID, MJ, ROSTKOWSKI, PM AND VOGELSANG, C. 2017.

Screening programme 2016-Selected compounds with relevance for EU regulation. NILU report.

SCHLABACH, M., ANDERSEN, M. S., GREEN, N., SCHØYEN, M. & KAJ, L. 2007. Siloxanes in the Environment of the Inner Oslofjord. *NILU OR,* 27**,** 2007.

SIJM, D. T., VERBERNE, M. E., DEJONGE, W. J., PART, P. & OPPERHUIZEN, A. 1995. Allometry in the uptake of hydrophobic chemicals determined in vivo and in isolated perfused gills. *Toxicology and applied pharmacology,* 131**,** 130-135.

TALALAY, P. 2007. Dimethyl siloxane oils as an alternative borehole fluid. *Annals of Glaciology,* 47**,** 82-88.

TRIEST, J. & ALEMANY, O. 2014. Drill fluid selection for the SUBGLACIOR probe: a review of silicone oil as a drill fluid. *Annals of Glaciology,* 55**,** 311-321.

WANG, D.-G., DU, J., PEI, W., LIU, Y. & GUO, M. 2015. Modeling and monitoring cyclic and linear volatile methylsiloxanes in a wastewater treatment plant using constant water level sequencing batch reactors. *Science of the Total Environment,* 512**,** 472-479.

WARNER, N. A., KROGSETH, I. S. & WHELAN, M. J. 2015. Comment on “Unexpected occurrence of volatile dimethylsiloxanes in Antarctic soils, vegetation, phytoplankton, and krill”. *Environmental science & technology,* 49**,** 7504-7506.

XU, L., SHI, Y. & CAI, Y. 2013. Occurrence and fate of volatile siloxanes in a municipal wastewater treatment plant of Beijing, China. *Water research,* 47**,** 715-724.

ZHANG, Z., QI, H., REN, N., LI, Y., GAO, D. & KANNAN, K. 2011. Survey of cyclic and linear siloxanes in sediment from the Songhua River and in sewage sludge from wastewater treatment plants, Northeastern China. Archives of environmental contamination and toxicology, 60, 204-211

9. Abbreviations

%	Percentage
°C	Degrees centigrade
B	Bioaccumulative
BCF	Bioconcentration factor
BMF	Biomagnification factor
CLP	Classification, labelling and packaging (of substances and mixtures)
C&L	Classification and labelling
cm	Centimetre
CMR	Carcinogen, Mutagen or Reprotoxic
CoRAP	Community Rolling Action Plan
CSA	Chemical Safety Assessment
CSR	Chemical Safety Report
CTD	Characteristic travel distance
d	Day
D4	Octamethylcyclotetrasiloxane
D5	Decamethylcyclopentasiloxane
DMEL	Derived Minimal Effect Level
DNEL	Derived No Effect Level
DOC	Dissolved Oxygen Content
DSC	Differential Scanning Calorimetry
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 Competent Authority
EPA	Environmental Protection Agency
ES	Exposure Scenario
ERC	Environmental release category (ERC)
EU	European Union
g	Gramme
GC	Gas chromatography
GC/FID	Gas chromatography – Flame Ionisation Detection
GC/MS (GC-MS)	Gas chromatography – mass spectrometry
GLP	Good laboratory practice
HMDS	Hexamethyldisiloxane (L2)
hPa	Hectopascal
ISO	International Organisation for Standardisation
IUCLID	International Uniform Chemical Information Database
IUPAC	International Union of Pure and Applied Chemistry
J	Joule
K	Kelvin
k_{obs}	Observed first order rate constant
kg	Kilogram
kJ	Kilojoule

km	Kilometre
kPa	Kilopascal
Koa	Octanol-air partition coefficient
Koc	Organic carbon-water partition coefficient
Kow	Octanol-water partition coefficient
L	Litre
L2	Hexamethyldisiloxane
L3	Octamethyltrisiloxane
L4	Decamethyltetrasiloxane
L5	Dodecamethylpentasiloxane
LEV	Local Exhaust Ventillation
Log	Logarithmic value
LOD	Limit of detection
LOQ	Limit of quantitation
LRT	Long range transport
M	Molar
m	Metre(s)
µg	Microgram
mg	Milligram
min	Minute
mL	Millilitre
mol	Mole
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
PDMS	Polydimethylsiloxane
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	Universal gas constant

r2	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
SSD	Species Sensitivity Distribution
t	Tonne
T	Toxic (hazard classification)
TE	Transfer efficiency
TMS	trimethyl silanol
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

L3 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 (L4) 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 40: Trends for PBT endpoints

	L2 EC 203-492-7	L3 EC 203-497-4	L4 EC 205-491-7	L5 EC 205-492-2
Persistence	increasing half-life →			
Bioaccumulation	← peaks at L3 →			
Toxicity 1(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.