Committee for Risk Assessment

RAC

Annex 1

Background document

to the Opinion proposing harmonised classification and labelling at EU level of

Octamethylcyclotetrasiloxane; [D4]

EC Number: 209-136-7
CAS Number: 556-67-2

CLH-O-0000001412-86-192/F

The background document is a compilation of information considered relevant by the dossier submitter or by RAC for the proposed classification. It includes the proposal of the dossier submitter and the conclusion of RAC. It is based on the official CLH report submitted to public consultation. RAC has not changed the text of this CLH report but inserted text which is specifically marked as 'RAC evaluation'. Only the RAC text reflects the view of RAC.

Adopted

9 March 2018

CLH report

Proposal for Harmonised Classification and Labelling

Based on Regulation (EC) No 1272/2008 (CLP Regulation),
Annex VI, Part 2

International Chemical Identification:

Octamethylcyclotetrasiloxane; D4

EC Number: **209-136-7**

CAS Number: **556-67-2**

Index Number: **014-018-00-1**

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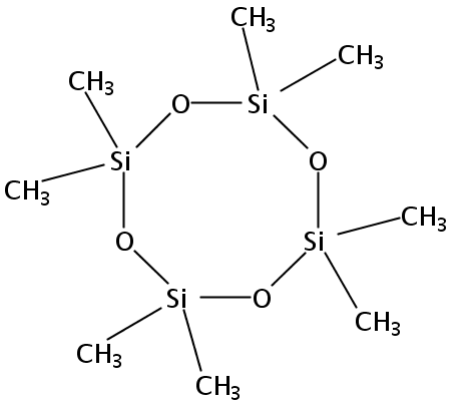
1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 1: Substance identity and information related to molecular and structural formula of the substance

Name(s) in the IUPAC nomenclature or other international chemical name(s)	Octamethylcyclotetrasiloxan
Other names (usual name, trade name, abbreviation)	D4
ISO common name (if available and appropriate)	-
EC number (if available and appropriate)	209-136-7
EC name (if available and appropriate)	octamethylcyclotetrasiloxane
CAS number (if available)	556-67-2
Other identity code (if available)	
Molecular formula	$C_8H_{24}O_4Si_4$
Structural formula	
SMILES notation (if available)	C[Si]1(C)O[Si](C)(C)O[Si](C)(C)O[Si](C)(C)O1
Molecular weight or molecular weight range	296.62 g/mol

1.2 Composition of the substance

Table 2: Constituents (non-confidential information)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)		Current self- classification and labelling (CLP)	
Octamethylcyclotetrasiloxane	For typical concentration and concentration ranges see confidential annex.	Repr. 2 Aquatic Chronic 4	H361f *** H413	Repr. 2 Aquatic Chronic 4 Flam. Liq. 3 Aquatic Chronic 2 Aquatic Chronic 1 Not Classified Acute Tox. 1 Acute Tox. 3 Acute Tox. 4 Acute Tox. 4	H361f *** H413 H226 H411 H410 - H330 H311 H302 H312

Table 3: Impurities (non-confidential information) if relevant for the classification of the substance

Impurity (Name and numerical identifier)	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)	The impurity contributes to the classification and labelling
Please refer to confidential annex.				

2 PROPOSED HARMONISED CLASSIFICATION AND LABELLING

2.1 Proposed harmonised classification and labelling according to the CLP criteria

Table 4:

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	014-018-00-1	octamethylcyclo-tetrasiloxane	209-136-7	556-67-2	Repr. 2 Aquatic Chronic 4	H361f*** H413	GHS08 Wng	H361f *** H413			
Dossier submitters proposal		octamethylcyclo-tetrasiloxane; D4			**Modify**: Aquatic Chronic 4 to Aquatic Chronic 1	**Modify**: H413 to H410	**Add**: GHS09	**Modify**: H413 to H410		**Add**: M=10	
Resulting Annex VI entry if agreed by RAC and COM					Repr. 2 Aquatic Chronic 1	H361f*** H410	GHS08 GHS09 Wng	H361f *** H410		M=10	

Table 5: Reason for not proposing harmonised classification and status under public consultation

Hazard class	Reason for no classification	Within the scope of public consultation
Explosives	Hazard class not assessed in this dossier	No
Flammable gases (including chemically unstable gases)	Hazard class not assessed in this dossier	No
Oxidising gases	Hazard class not assessed in this dossier	No
Gases under pressure	Hazard class not assessed in this dossier	No
Flammable liquids	Hazard class not assessed in this dossier	No
Flammable solids	Hazard class not assessed in this dossier	No
Self-reactive substances	Hazard class not assessed in this dossier	No
Pyrophoric liquids	Hazard class not assessed in this dossier	No
Pyrophoric solids	Hazard class not assessed in this dossier	No
Self-heating substances	Hazard class not assessed in this dossier	No
Substances which in contact with water emit flammable gases	Hazard class not assessed in this dossier	No
Oxidising liquids	Hazard class not assessed in this dossier	No
Oxidising solids	Hazard class not assessed in this dossier	No
Organic peroxides	Hazard class not assessed in this dossier	No
Corrosive to metals	Hazard class not assessed in this dossier	No
Acute toxicity via oral route	Data conclusive but not sufficient for classification	No
Acute toxicity via dermal route	Data conclusive but not sufficient for classification	No
Acute toxicity via inhalation route	Data conclusive but not sufficient for classification	No
Skin corrosion/irritation	Data conclusive but not sufficient for classification	No
Serious eye damage/eye irritation	Data conclusive but not sufficient for classification	No
Respiratory sensitisation	Data lacking	No
Skin sensitisation	Data conclusive but not sufficient for classification	No
Germ cell mutagenicity	Data conclusive but not sufficient for classification	No
Carcinogenicity	Data conclusive but not sufficient for classification	No
Reproductive toxicity	No change of the harmonised classification as Repr. 2 (H361f***)	No
Specific target organ toxicity-single exposure	Hazard class not assessed in this dossier	No
Specific target organ toxicity-repeated exposure	Data conclusive but not sufficient for classification	No
Aspiration hazard	Hazard class not assessed in this dossier	No
Hazardous to the aquatic environment	Harmonised classification proposed	**Yes**
Hazardous to the ozone layer	Hazard class not assessed in this dossier	No

3 HISTORY OF THE PREVIOUS CLASSIFICATION AND LABELLING

D4 has been classified as Repr. Cat. 3; R62 and R53 and added to Annex I of Directive 67/548/EEC in 2001 by the 28.ATP. With implementation of the CLP Regulation, D4 was classified and labelled with Repr. 2 (H361f***) and Aquatic Chronic 4 (H413).

4 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

- Change in existing entry due to changes in the criteria
- Differences in self-classification
- Disagreement by the dossier submitter with current self-classification

5 IDENTIFIED USES

The following information is taken from the InfoCard of D4 on the ECHA-website (ECHA, 2016b):

This substance is used in the following products: washing & cleaning products, polishes and waxes, cosmetics and personal care products, lubricants and greases, textile treatment products and dyes, leather treatment products, semiconductors and non-metal-surface treatment products. This substance has an industrial use resulting in manufacture of another substance (use of intermediates).

This substance is used in the following areas: formulation of mixtures and/or re-packaging. This substance is used for the manufacture of: chemicals, rubber products, plastic products, mineral products (e.g. plasters, cement) and electrical, electronic and optical equipment.

6 DATA SOURCES

- Registration dossiers (ECHA, 2016a)
- MSC opinion and Annexes (ECHA, 2015)
- PBT/vPvB evaluation factsheet (Environment Agency, 2013)

7 PHYSICOCHEMICAL PROPERTIES

Table 6: Summary of physicochemical properties

Property	Value	Reference	Comment (e.g. measured or estimated)
Physical state at 20°C and 101,3 kPa	liquid	Visual observation	
Melting/freezing point	17.7 °C	J. Amer. Chem. Soc., 75, 2227	Handbook data
Boiling point	175 °C	J Amer. Chem. Soc., 68, 358	Handbook data
Relative density	0.95g/cm³ at 25 °C	AIChE DIPPR Database	Handbook data
Vapour pressure	132 Pa at 25 °C	AIChE DIPPR Database	Handbook data
Surface tension			In accordance with Column 2 of REACH Annex VII, the surface tension study does not need to be conducted as the water solubility of the substance is less than 1 mg/l.
Water solubility	0.0562 mg/L At 23 °C and pH ca. 7	Environmental Toxicology and Chemistry, Vol. 15, No. 8, pp. 1263–1265	Measured
Partition coefficient n-octanol/water	6.488 at 25.1 °C	REACH registration dossier: Study according to OECD Guideline 123 (Partition Coefficient (1-Octanol / Water), Slow-Stirring Method), report date 2007. [ECHA (2016a)]	Measured
Granulometry			In accordance with Column 2 of REACH Annex VII, the granulometry study does not need to be conducted as the substance is marketed and used in a non-solid form.
Stability in organic solvents and identity of relevant degradation products			In accordance with Column 1 of REACH Annex IX this test is only required if stability of the substance is condered to be critical.
Dissociation constant			In accordance with section 1 of REACH Annex XI, the study does not need to be conducted because there are no ionizable groups present in the molecule.
Viscosity	1.6 mm²/s (kinematic) at 20 °C		QSAR MPBPVP v1.43 (EPIWIN 2009 and Stein 1994)

8 EVALUATION OF PHYSICAL HAZARDS

Not addressed in this dossier.

9 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

Not addressed in this dossier.

10 EVALUATION OF HEALTH HAZARDS

During the preparation of the CLH dossier the registration data and the 'Opinion on cyclomethicone D4/D5 (22 June 2010)' of the SCCS (Scientific Committee on Consumer Safety) (SCCS/1241/10, 2010) for carcinogenicity, mutagenicity, reproductive toxicity and respiratory sensitisation were checked which is evaluated with reliability 4 (secondary source). However, it was concluded that the registrants' and SCCS evaluation of the reliabilities of the studies is appropriate.

As a result of this evaluation the dossier submitter concludes that no additional classification regarding human health or change of the current harmonized classification as Repr. 2, H361f*** is required. Therefore no data are presented in Section 10 'Evaluation of health hazards'.

11 EVALUATION OF ENVIRONMENTAL HAZARDS

11.1 Rapid degradability of organic substances

Table 7: Summary of relevant information on rapid degradability

Method	Results	Remarks	Reference
OECD Guideline 111 (Hydrolysis as a function of pH)	pH 4: half-life = 4.76 hours (at 9.5 °C) half-life = 1.77 hours (at 24.6 °C) half-life = 0.885 hours (at 35.1 °C) pH 7: half-life = 542 hours (at 9.5 °C) half-life = 91.4 hours (at 24.6 °C) half-life = 144 hours (at 24.6 °C) half-life = 69.3 hours (at 24.8 °C) half-life = 24.9 hours (at 35 °C) pH 9: half-life = 6.37 hours (at 9.5 °C) half-life = 5.61 hours (at 9.5 °C) half-life = 0.902 hours (at 24.6 °C) half-life = 1.01 hours (at 24.3 °C) half-life = 0.190 hours (at 34.5 °C) half-life = 0.218 hours (at 34.6 °C) degradation product: dimethylsilanediol (CAS: 1066-42-8) 12°C, pH 7; half-life = 16.7 days (freshwater) 9°C, pH 8; half-life = 2.9 days (marine water)	Rel. 1 GLP-study	(ECHA, 2015, 2016a)
OECD Guideline 111 (Hydrolysis as a function of pH)	25°C pH 4 half-life = 33 hours pH 7 half-life = 69 hours pH 9 half-life = 0.56 hours	Rel. 4 – secondary source - No GLP-study - tested at only one temperature - not further considered for C&L	(ECHA, 2016a)
OECD Guideline 310 (CO2 in sealed vessels – Headspace Test)	3.7 % CO_2 evolution after 29 days	Rel. 1 GLP-study	(ECHA, 2015, 2016a)
OECD Guideline 308 (Aerobic and anaerobic transformation in	24°C half-life = 242 days (aerobic conditions)	Rel. 4 – secondary source) GLP-study	(ECHA, 2015)

Method	Results	Remarks	Reference
aquatic sediment system)			

11.1.1 Ready biodegradability

Ready biodegradation of D4 was investigated in a study conducted according to OECD Guideline 310 using 10 mg solids/L inoculum (activated sludge, sewage, soil) and 10 mg/L test substance. After 29 days 3.7 % CO_2 evolution was observed. CO_2 evolution of the reference substance (sodium benzoat) was 87.73 % after 14 days. 50.76 % CO_2 evolution at day 14 was shown in the toxicity control. In conclusion, D4 is not readily biodegradable.

11.1.2 BOD_5/COD

No data available.

11.1.3 Hydrolysis

The hydrolysis of D4 was tested according to OECD Guideline 111 at pH 4,7, and 9. The average half-life for pH7 at 25°C was calculated by the registrant to be 3.9 days (ECHA, 2016a). Nevertheless, based on Annex II of the guidance on the application of CLP criteria, the degree of degradation depends not only on the intrinsic degradability but also on the environmental conditions. Hydrolysis was tested in clean water test system. D4 is highly adsorptive to organic matter, which is preventing the hydrolytic degradation in natural waters. Furthermore, the average surface water temperature of 12°C is a more realistic environmental condition in Europe than 25°C. The half-life for the lower temperature was estimated to be 16.7 days (pH 7) (ECHA, 2015).

11.1.4 Other convincing scientific evidence

No data available.

11.1.4.1 Field investigations and monitoring data (if relevant for C&L)

Not relevant for this dossier.

11.1.4.2 Inherent and enhanced ready biodegradability tests

No data available.

11.1.4.3 Water, water-sediment and soil degradation data (including simulation studies)

Sediment:
Based on OECD Guideline 308 sediment simulation studies, D4 has an estimated degradation half-life of 242 days in aerobic sediment at 24°C (expected to be longer at lower temperatures) (ECHA, 2015). Low degradation in sediment is also supported by sediment core data from Lake Pepin, USA (monitoring data, (ECHA, 2015)).

Soil:
The available data do not allow a reliable soil degradation half-life to be derived.

11.1.4.4 Photochemical degradation

Not relevant for this dossier.

11.2 Environmental transformation of metals or inorganic metals compounds

Not relevant for this dossier.

11.2.1 Summary of data/information on environmental transformation

Not relevant for this dossier.

11.3 Environmental fate and other relevant information

In a reliable study according to OECD Guideline 106 a mean log Koc of 4.22 (average of three different soils; 24.8°C) was observed. It is therefore likely that D4 will adsorb strongly to organic matter in sediment and soil. The Henry´s law constant of 1.21 x 10^6 Pa*m³/mol at 21.7 °C indicates a high potential for volatilization from water (ECHA, 2016a).

11.4 Bioaccumulation

Table 8: Summary of relevant information on bioaccumulation

Method	Results	Remarks	Reference
OECD Guideline 123	Log Kow = 6.488 at 25.1 °C	Rel. 2 GLP-study	(ECHA, 2015, 2016a)
EPA OTS 797.1520 (*Pimephales promelas*) ^{14}C measurement	BCF = 12400 L/kg (steady state) BCF = 13400 L/kg (kinetic) Re-analysis of the data: BCF = 19000 L/kg (kinetic) BCF = 14900 L/kg (kinetic, lipid normalised)	Rel. 1 GLP-study	(ECHA, 2015, 2016a)
OECD Guideline 305 (Cyprinus carpio	BCF = 3129 L/kg (steady state, 2.52 µg/L) BCF = 3000 L/kg (steady state, 0.22 µg/L) (lipid content close to 5%)	Rel. 2 GLP-study	(ECHA, 2015, 2016a)
OECD Guideline 305 (Cyprinus carpio)	BCF = 3329 L/kg (steady state, 2.4 µg/L treatment level) BCF = 3967 L/kg (steady state, 0.23 µg/L treatment level) BCF = 4106 L/kg (kinetic, 2.4 µg/L) BCF = 5540 L/kg (kinetic, 0.23 µg/L) (lipid content close to 5%)	Rel. 2 GLP-study	(ECHA, 2015, 2016a)

11.4.1 Estimated bioaccumulation

Not data available.

11.4.2 Measured partition coefficient and bioaccumulation test data

A log Kow of 6.488 was determined at 25.1°C according to OECD Guideline 123 (ECHA, 2016a).

The bioconcentration factor (BCF) of D4 was measured (based on ^{14}C measurements) for *Pimephales promelas* using EPA OTS 797.1520 (ECHA, 2015, 2016a). The study included a preliminary test with 6 days exposure followed by 14 days of depuration and a definitive test with 28 days of exposure and 14 days of depuration. A steady-state BCF of 12400 L/kg after 28 days and a kinetic BCF of 13400 L/kg was reported. The data of the study were re-analyzed to take the variable exposure concentrations during the tests into account (concentration in the range of 0.2 to 0.5 µg/L) (Smit et al., 2012). The re-analysis resulted in a kinetic lipid-normalized BCF of 14900 L/kg (lipid content = 6.4 %).

Furthermore, two bioconcentration studies with *Cyprinus carpio* are available (ECHA, 2015, 2016a). Both studies were carried out according to OECD Guideline 305 and had an exposure period of 60 days followed by a depuration period of 15 days in the first study and 12 days in the second. The lipid content in both studies were close to 5 %.

The first study was carried out using two exposure concentrations (0.22 µg/L and 2.52 µg/L) in a continuous-flow system. The concentration in the fish was found to reach steady state within 39 days. The steady-state BCF values were 3129 L/kg for the higher exposure level and 3000 L/kg for the lower exposure level.

The second study with *Cyprinus carpio* was carried out using 0.23 µg/L and 2.4 µg/L D4. Steady state was found to have been reached by day 46. The mean BCF at steady state was 3329 L/kg at the 2.4 µg/L treatment level and 3967 L/kg at the 0.23 µg/Ltreatment level. Based on the uptake rate constant (k_1) of 407 L/kg/day and the overall depuration rate constant (k_2) of 0.0991 day^{-1}, a kinetic BCF of 4106 L/kg was estimated for the 2.4 µg/L treatment level. For the 0.23 µg/L treatment level a kinetic BCF of 5540 L/kg was determined (k_1 = 467 L/kg/day, k_2 = 0.0843 day^{-1}).

Based on measured BCF values and log Kow, D4 has a high bioaccumulation potential.

11.5 Acute aquatic hazard

Only the most reliable studies are included in the report. There are other studies available from the registration dossier (ECHA, 2016a).

Table 9: Summary of relevant information on acute aquatic toxicity

Method	Species	Test material	Results[1]	Remarks	Reference
EPA 797.1400	*Oncorhynchus mykiss*	CAS 556-67-2	96h-LC_{50} > 22 µg/L (mean measured) 96h-NOEC ≥ 22 µg/L (mean measured) 14d-NOEC = 4.4 µg/L (mean measured)	Prolonged acute tox. study Rel. 1 GLP-study	(Sousa et al., 1995)
EPA 797.1300	*Daphnia magna*	CAS 556-67-2	48h-EC_{50} > 15 µg/L (mean measured)	Rel. 1 GLP-study	(Sousa et al., 1995)
EPA 797.1050	*Selenastrum capricornutum (*new: *Pseudokirchneriella subcapitata)*	CAS 556-67-2	96h-ErC_{50} > 22 µg/L (initially measured) (corresponds to 6 µg/L mean measured)	Rel. 2 GLP-study	(ECHA, 2016a)

11.5.1 Acute (short-term) toxicity to fish

(Sousa et al., 1995) conducted two reliable (prolonged) acute toxicity tests to fish, one with *Oncorhynchus mykiss* and one with *Cyprinodon variegatus*. As there were no effects with the latter one, only the test with *O.mykiss* will be described here. The test was performed according to EPA Guideline 797.1400 at 12 ± 2 °C. Sealed glass vessels were used as D4 is volatile. Five concentrations (2.9, 4.4, 6.9, 12 and 22 µg/L measured) were used with two replicates each and ten organisms per vessel (flow-through). No vehicle was used. The biomass loading rate was 0.17 g/L. A photoperiod of 16 h light per day with a light intensity of 55 to 210 footcandles was obtained. Up to day 7 no effects were observed. Therefore, the 96h-EC_{50} was > 22 µg/L. At day 14 20 % of the organisms in test concentration 6.9 µg/L died. Therefore, the 14d-NOEC for survival is 4.4 µg/L.

With *C.variegatus* concentrations up to 6.3 µg/L (maximum achievable concentration) were tested in the (prolonged) acute toxicity test and no effects were observed. Therefore the 14d-NOEC is 6.3 µg/L.

11.5.2 Acute (short-term) toxicity to aquatic invertebrates

(Sousa et al., 1995) also conducted two reliable tests with aquatic invertebrates (freshwater: *Daphnia magna* and marine: *Mysidopsis bahia*, new name: *Americamysis bahia*). They were performed according to EPA 797.1300 and EPA 797.1930. The *D.magna* test was a flow-through test with a duration of 48 hours and analytical monitoring. The test concentrations were 1.7, 2.9, 3.7, 7.8 and 15 µg/L (measured). No vehicle was used. There was no effect observed up to the highest test concentration. Therefore, the 48h-EC_{50} was > 15 µg/L.

With *Americamysis bahia* the test was conducted 96 hours (flow-through) without vehicle with test concentrations of 1.3, 2.2, 3.7, 6.9 and 9.1 µg/L (measured). No effects up to the highest test concentration were observed. Therefore, the 96h-LC_{50} was > 9.1 µg/L.

11.5.3 Acute (short-term) toxicity to algae or other aquatic plants

In (ECHA, 2016a) an toxicity test to algae is reported. The test was performed according to EPA Guideline 797.1050 with *Selenastrum capricornutum* (new: *Pseudokirchneriella subcapitata*). It was a limit test with sealed test vessels without headspace. The limit concentration was 22 µg/L (initially measured) (corresponds to 6 µg/L mean measured concentration). No vehicle was used. The test was valid as the criteria of the guideline OECD 201 (biomass concentration in the control cultures should have increased by a factor of at least 16 within 72h) was fulfilled (increased cell density by a factor of 16.5 after 72 h in the control group). The cell density was decreased 18 % in the treatment compared with the control group. The cell density in both (test system and control system) was lower than expected. In the test also an open-system reference control system was included which demonstrated that the restricted gaseous exchange in the sealed system caused a reduction in growth rate.

11.5.4 Acute (short-term) toxicity to other aquatic organisms

Not data available.

11.6 Long-term aquatic hazard

Table 10: Summary of relevant information on chronic aquatic toxicity

Method	Species	Test material	Results[1]	Remarks	Reference
40 CFR 797.1600	*Oncorhynchus mykiss*	CAS 556-67-2	93d-NOEC ≥ 4.4 µg/L (mean measured)	Rel. 1 GLP-study	(ECHA, 2016a; Sousa et al., 1995)
EPA 797.1400	*Oncorhynchus mykiss*	CAS 556-67-2	14d-NOEC = 4.4 µg/L 14d-LOEC = 6.9 µg/L (both mean measured)	Prolonged acute tox. study Rel. 1 GLP-study	(Sousa et al., 1995)
EPA 797.1330	*Daphnia magna*	CAS 556-67-2	21d-NOEC = 7.9 µg/L (mean measured)	Rel. 1 GLP-study	(Sousa et al., 1995)
EPA 797.1050	*Selenastrum capricornutum (*new: *Pseudokirchneriella subcapitata)*	CAS 556-67-2	96h-NOErC < 22 µg/L (initially measured) (corresponds to 6 µg/L mean measured)	Rel. 2 GLP-study	(ECHA, 2016a)

11.6.1 Chronic toxicity to fish

Additionally to the prolonged acute toxicity study with *O.mykiss*, (Sousa et al., 1995) also conducted a reliable long-term (93 day) fish early life stage toxicity study . The test was performed according to Guideline 40 CFR 797.1600 with analytical monitoring and without the use of a vehicle. It was a flow-through test with five concentrations (0.25, 0.53, 1.1, 1.9 and 4.4 µg/L, measured). The resulting NOEC from the FELS test was ≥ 4.4 µg/L (measured). This was the highest test concentration. In a prolonged acute toxicity study with *Oncorhynchus mykiss* also conducted by (Sousa et al., 1995) mortality occurred at a next higher concentration of 6.9 µg/L. It cannot be ruled out that effects might have been observed at higher concentrations than tested in the FELS test. Generally, a longer-term test with early life stages is preferable to a prolonged acute test for the purposes of chronic toxicity assessment. However, the two studies did not overlap in test concentration, so the true level of toxicity to fish over the long-term is unclear.

Overall, the long-term NOEC for fish is assumed to be around 4--6 µg/L, although there is some uncertainty in the actual value and the reasons for the differences between the two studies.

11.6.2 Chronic toxicity to aquatic invertebrates

(Sousa et al., 1995) carried out a reliable 21 day reproduction study with *Daphnia magna* using a flow-through system with no head space (to minimise loss of D4 through volatilisation). The D4 tested was > 99 % pure and stock solutions of the substance were prepared by slow-stirring dilution water with a floating layer (approximately 6 mm thick) of D4. This method of stock-solution preparation gives reproducible results and can achieve a maximum concentration of ca. 15 µg/L in hard freshwater. Five exposure concentrations were used (measured concentrations were 1.7, 1.8, 4.2, 7.9, and 15 µg/L). This study showed a statistically significant (p = 0.05) reduction in the survival at the highest concentration tested (survival in the 15 µg/L was 77 %) compared with the control population (survival was 93 %) after 21 days. The 21-day NOECsurvival was therefore 7.9 µg/L. For the reproduction endpoint, the mean cumulative number of offspring per female daphnid was 111 in the control, 107, 92, 123, 151, and 167 in the 1.7, 1.8, 4.2, 7.9 and 15 µg/L treatment groups, respectively. There were no statistically significant (p = 0.05) differences between the control response and the treatment response in the 1.7, 1.8, and 4.2 µg/L groups, but the mean cumulative number of offspring per female was significantly higher in the 7.9 µg/L treatment group than in the control groups (the data for the 15 µg/L treatment group were not included in the statistical analysis as a reduction in daphnid survival occurred in this group). Therefore it is concluded that concentrations of D4 ≤ 7.9 µg/L do not adversely affect the reproduction of *D. magna*.

11.6.3 Chronic toxicity to algae or other aquatic plants

As described above (chapter 11.5.3), there is one toxicity study with algae reported in (ECHA, 2016a). As it is a limit test, the validity of the study is restricted. The resulting NOEC is < 22 µg/L (initially measured) (corresponds to 6 µg/L mean measured).

11.6.4 Chronic toxicity to other aquatic organisms

Not data available.

11.7 Comparison with the CLP criteria

11.7.1 Acute aquatic hazard

Table 11: Comparison with critera for acute aquatic hazards

	Criteria for environmental hazards	D4	Conclusion
Acute Aquatic Toxicity	Cat. 1: $LC_{50}/EC_{50}/ErC_{50} \leq 1$ mg/L	Fish: 96h-LC_{50} > 0.022 mg/L (mean measured) Invertebrates: 48h-EC_{50} > 0.015 mg/L (mean measured) Algae: 96h-ErC_{50} > 0.022 mg/L (initally measured)	**No classification**

11.7.2 Long-term aquatic hazard (including bioaccumulation potential and degradation)

Table 12: Comparison with critera for long-term aquatic hazards

	Criteria for environmental hazards	D4	Conclusion
Rapid Degradation	Half-life hydrolysis < 16 days Readily biodegradable in a 28-day test for ready biodegradability (> 70% DOC removal or > 60% theoretical oxygen demand, theoretical carbon dioxide) Supporting information: Half-life aquatic sediment < 16 days	Half-life hydrolysis = 16.7 days (pH7, 12°C) 3.7 % after 29 days (CO_2 evolution) => not readily biodegradable Half-life = 242 days	**Not rapidly degradable**
Bioaccumulation	Log Kow ≥ 4 BCF ≥ 500	Log Kow = 6.488 BCF = 3000-14900	**High potential for bioaccumulation**
Aquatic Toxicity	Non-rapidly degradable substances: Cat. 1: NOEC ≤ 0.1 mg/L Cat. 2: NOEC ≤ 1 mg/L	Fish: 14d-NOEC = 0.0044 mg/L (mean measured) Invertebrates: 21d-NOEC = 0.0079 mg/L (mean measured) Algae: 96h-NOErC < 0.022 mg/L (initially measured)	**Aquatic chronic 1, H410, M=10** (based on 21d-$NOEC_{Daphnia}$ = 0.0079 mg/L suppored by 14d-$NOEC_{fish}$= 0.0044 mg/L)

11.8 CONCLUSION ON CLASSIFICATION AND LABELLING FOR ENVIRONMENTAL HAZARDS

D4 is not rapidly degradable and fulfills therefore with a NOEC ≤ 0.1 mg/L the classification criteria for hazardous to the aquatic environment “Aquatic Chronic 1”. The hazard statement code is H410. With the NOECs of 0.0044 mg/L (for fish) and 0.0079 mg/L (for aquatic invertebrates) a M-factor of 10 has to be assigned.

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

Octamethylcyclotetrasiloxane (D4) is classified as Aquatic Chronic 4 in Annex VI of the CLP Regulation. The Dossier Submitter (DS) proposed to classify D4 as Aquatic Chronic 1; H410, based on its high potential for bioaccumulation, no rapid degradation and chronic NOEC values ≤ 0.1 mg/L. An M-factor of 10 was also proposed by the DS due to the NOEC value of 0.0044 mg/L for fish and 0.0079 mg/L for aquatic invertebrates, respectively.

Degradation

There was one ready biodegradability test available on D4 (OECD TG 310, GLP) using 10 mg solids/L inoculum (activated sludge, sewage, soil) and 10 mg/L (based on DOC) test substance. After 29 days, 3.7 % CO_2 evolution was observed indicating that the substance is not readily biodegradable. No microbial toxicity of D4 was indicated by CO_2 evolution of 54 % after 29 days from toxicity control (degradation was > 25% after 14 days) (REACH Registration dossier).

The hydrolysis of D4 was tested at 10, 25 and 35 °C and at pH 4, 7, and 9 (OECD TG 111, GLP). The average half-life at pH 7 and 25 °C was calculated to be 3.9 days. At pH 4 the half-life was 1.77 hours and at pH 9 0.902 hours at 24.6 °C. At pH 6.99 and 9.5 °C the half-life was 542 hours (~23 days) and at pH 7 and 12 °C the estimated half-life was 16.7 days. The DS also reported a half-life of 2.9 days at pH 8 and 9 °C in marine water in the CLH Report. According to the DS, one of the degradation products was dimethylsilanediol (CAS 1066-42-8) which has not been self-classified for environmental hazard by any of the 49 notifiers in the ECHA C&L Inventory. The full study report of the above mentioned OECD TG 111 study was provided after the Public Consultation. In addition to half-lives, the study also analysed kinetic data. It has been demonstrated that, at concentrations below the limit of solubility, D4 was readily transformed via hydrolysis to a smaller, more polar compound, likely dimethylsilanediol ($Me_2Si(OH)_2$). This probably occurs through a series of consecutive irreversible (pseudo) first-order reactions that follows formation of tetramer diol.

Based on an OECD TG 308 (GLP) test, D4 had an estimated degradation half-life of 242 days in aerobic sediment at 24 °C which is expected to be longer at lower temperatures. The major degradation products were hydrolytic products, such as dimethylsilanediol and non-extractable silanols while $^{14}CO_2$ generation was minimal, indicating that complete mineralisation of D4 or its degradation products is very slow. D4 degradation in non-sterilised samples was significantly faster than that in the chemically sterilised samples, suggesting that the degradation of D4 in the sediment might not be purely abiotic (REACH Registration dossier). There was no data on photodegradation available in the CLH Report because they were not seen as relevant.

Bioaccumulation

A Log K_{ow} of 6.488 was determined at 25.1 °C in an OECD TG 123 study (GLP). There were three fish bioconcentration studies available. In the first study the bioconcentration factor (BCF) was measured based on ^{14}C measurements for *Pimephales promelas*

following EPA OTS 797.1520 (GLP). The study included a preliminary test with 6 days exposure followed by 14 days of depuration and a definitive test with 28 days of exposure and 14 days of depuration. A steady-state BCF of 12 400 L/kg after 28 days and a kinetic BCF of 13 400 L/kg was reported. The data of the study were re-analysed to take the variable exposure concentrations during the tests into account (concentration in the range of 0.2 to 0.5 µg/L. The re-analysis resulted in a kinetic lipid-normalised BCF of 14 900 L/kg (lipid content = 6.4 %).

The two other studies were carried out according to OECD TG 305 (GLP) with *Cyprinus carpio* and had an exposure period of 60 days followed by a depuration period of 15 days in the first study and 12 days in the second. The lipid content in both studies was close to 5 %. The first study was carried out using two exposure concentrations (0.22 µg/L and 2.52 µg/L) in a continuous-flow system. The concentration in the fish was found to reach steady state within 39 days. The steady-state BCF values were 3 129 L/kg for the higher exposure level and 3 000 L/kg for the lower exposure level. The second study with *Cyprinus carpio* was carried out using 0.23 µg/L and 2.4 µg/L of D4. Steady state was reached by day 46. The mean BCF at steady state was 3 329 L/kg at the higher exposure level and 3 967 L/kg at the lower. A kinetic BCF of 4 106 L/kg was estimated for the higher treatment level and 5 540 L/kg for the lower.

Acute toxicity

The measured water solubility of D4 was 0.0562 mg/L at 23 °C and pH ca. 7. The Henry's law constant of 1.21 × 10^6 Pa×m^3/mol at 21.7 °C indicated a high potential for volatilization from water surface.

Table : Summary of relevant information on acute aquatic toxicity (including also data from the most recently updated REACH Registration dossier (October 2017))

Method	Species	Test conditions	Results	Remarks	Reference
EPA 797.1400, GLP	*Oncorhynchus mykiss*	flow-through sealed system, freshwater, 12 °C, pH 6.5-7.2	96 h LC_{50} > 22 µg/L (mm) no effects; 14 d LC_{50} = 10 µg/L mm (1) 14 d NOEC = 4.4 µg/L (mm)	Prolonged acute tox. study.	Anonymous, 1995
EPA 797.1400, GLP	*Cyprinodon variegatus*	flow-through sealed system, seawater (salinity 20 ppm), 25±2°C, pH 7.9-8.1	96 h LC_{50} > 6.3 µg/L (mm) 14 d LC_{50} > 6.3 µg/L mm, no effects 14 d NOEC ≥ 6.3 µg/L (mm)	Prolonged acute tox. study	REACH Registration dossier 10/2017
EPA 797.1300, GLP	*Daphnia magna*	flow-through, freshwater, 20±2°C, pH 7.3-7.9	48 h EC_{50} > 15 µg/L (mm) no effects		Sousa *et al*. 1995

EPA 797.1930, GLP	*Americamysis bahia*	flow-through, salt water (salinity 20 ppm), 25±2°C, pH 7.4-8.1	96 h LC_{50} > 9.1 µg/L (mm) no effects		REACH Registration dossier 10/2017
EPA 797.1050, GLP	*Selenastrum capricornutum* (new: *Pseudokirchneriella subcapitata)*	limit test; freshwater; sealed, no headspace; 23-24°C, pH 7.5-10	96 h E_rC_{50} > 6 µg/L (mm, corresponding 22 µg/L im)		ECHA 2016a

(1) Data from REACH Registration dossier 10/2017
im = initially measured
mm = mean measured

There were two reliable prolonged acute toxicity tests to fish, one with *Oncorhynchus mykiss* and one with *Cyprinodon variegatus*. The *Oncorhynchus mykiss* test was performed according to EPA Guideline 797.1400 at 12 ± 2 °C. Sealed glass vessels were used as D4 is volatile. Five concentrations (2.9, 4.4, 6.9, 12 and 22 µg/L mean measured) were used with two replicates each and ten organisms per vessel (flow-through). No vehicle was used. In contrast to the OECD TG 203 (average fish size: 5 ± 1 cm), the fish had an average size of only 3.7 cm. The biomass loading rate was 0.17 g/L. Up to day 7, no effects were observed. Therefore, the 96 h EC_{50} was > 22 µg/L (mean measured). At day 14, 20 % of the organisms in test concentration 6.9 µg/L died. Therefore, the 14 d NOEC for survival was 4.4 µg/L. In the flow-through test (EPA 797.1400) with *Cyprinodon variegatus*, concentrations up to 6.3 µg/L (maximum achievable concentration) were tested in the prolonged acute toxicity test and no effects were observed. Therefore, the 14 d NOEC was 6.3 µg/L. The test was performed in salt water (salinity 20 ppt), at 25 °C, and at pH 7.9-8.1 (REACH Registration dossier).

Two reliable tests with aquatic invertebrates (freshwater: *Daphnia magna* and marine: *Mysidopsis bahia*, new name: *Americamysis bahia*) were conducted. They were performed according to EPA 797.1300 and EPA 797.1930. The *Daphnia magna* test was a flow-through test with a duration of 48 hours and analytical monitoring. The test concentrations were 1.7, 2.9, 3.7, 7.8 and 15 µg/L (mean measured). No vehicle was used. There was no effect observed up to the highest test concentration. Therefore, the 48 h EC_{50} was > 15 µg/L. With *Americamysis bahia* the test was conducted 96 hours without vehicle with test concentrations of 1.3, 2.2, 3.7, 6.9 and 9.1 µg/L (mean measured) in salt water (20 ppt solubility). No effects up to the highest test concentration were observed. Therefore, the 96 h LC_{50} was > 9.1 µg/L.

There is an algae test available. The test was performed according to EPA Guideline 797.1050 with *Selenastrum capricornutum* (new: *Pseudokirchneriella subcapitata*). It was a limit test with sealed test vessels without headspace. The limit concentration was 22 µg/L (initial measured) (corresponds to 6 µg/L mean measured concentration). No vehicle was used. Despite the fact being performed according to EPA standards, the validity criteria of OECD TG 201 were fulfilled. The cell density was decreased 18 % in the treatment compared with the control group. The cell density in both (test system and control system) was lower than expected. In the test also an open-system reference

control system was included, which demonstrated that the restricted gaseous exchange in the sealed system caused a reduction in growth rate.

The Dossier Submitter concluded that no short-term (acute) aquatic hazard classification is necessary for D4 because no effects were shown at the highest concentrations tested in the acute toxicity test.

Chronic toxicity

Table. Summary of relevant information on chronic aquatic toxicity

Method	Species	Test material	Results	Remarks	Reference
40 CFR 797.1600, GLP	*Oncorhynchus mykiss*	flow-through, closed system, freshwater, 12 °C, pH 6.8-7.5	93 d NOEC ≥ 4.4 µg/L (mm)	No effects at highest test concentration.	ECHA 2016a; Anonymous, 1995
EPA 797.1400, GLP	*Oncorhynchus mykiss*	flow-through sealed system, freshwater, 12 °C, pH 6.5-7.2	14 d NOEC = 4.4 µg/L (mm) 14 d LOEC = 6.9 µg/L (mm)	Prolonged acute tox. study.	Anonymous, 1995
OECD 204 (3) GLP	*Oncorhynchus mykiss*	flow through, fresh water, 11.5-12.5 °C, pH 7.3-7.7	14 d LC_{50} = 17 µg/L (mm) 14 d NOEC = 6.8 µg/L (mm)	Prolonged acute tox. study Fish average wet weight 0.12 g	REACH Registration dossier 10/2017
EPA 797.1330, GLP	*Daphnia magna*	flow-through, freshwater, 19-22 °C, pH 6.6-7.6	21 d NOEC = 7.9 µg/L (mm) (survival); 21 d NOEC ≥ 15 µg/L (growth and reproduction)(1)		Sousa *et al*. 1995
EPA 797.1050, GLP	*Selenastrum capricornutum* (new: *Pseudokirchneriella subcapitata*)	limit test; freshwater; sealed, no headspace; 23-24 °C, pH 7.5-10	96 h NOE_rC > 6 µg/L (mm, corresponding 22 µg/L as im) recalculated: E_rC_{10} > 22 µg/L(2) im		ECHA 2016a

(1) Data from REACH Registration dossier 10/2017
(2) Public Consultation
(3) Study received after the Public Consultation, also included in the REACH Registration dossier 10/2017
im = initially measured
mm = mean measured

In addition to the prolonged acute toxicity study with *Oncorhynchus mykiss*, described in relation to acute toxicity, a full study report on fish prolonged acute toxicity was submitted during the RAC evaluation. This GLP study was performed according to OECD 204 Guideline with *Oncorhynchus mykiss* under flow-through test conditions. Five concentrations were tested (1.9, 3.4, 6.8, 13 and 29 µg/L, mean measured representing 54, 49, 49, 46 and 52 % of the nominal) at pH 7.3-7.7 and 11.5-12.5 °C. Mortality in the 13 and 29 µg/L was 25 % and 90 %, respectively. The 14-day LC_{50} value was calculated to be 17 µg/L and the NOEC was 6.8 µg/L.

One reliable long-term fish early life stage toxicity (FELS) study was available. The test was performed according to Guideline 40 CFR 797.1600 with analytical monitoring and without the use of a vehicle. Test temperature was 12 ± 2°C. It was a flow-through test with five concentrations (0.25, 0.53, 1.1, 1.9 and 4.4 µg/L, measured). The resulting NOEC from the FELS test was ≥ 4.4 µg/L (mean measured), the highest concentration tested for embryo viability, hatching success, larval survival and growth (REACH Registration dossier). On the other hand in a prolonged acute toxicity study with *Oncorhynchus mykiss,* mortality occurred at the next highest concentration of 6.9 µg/L. It cannot be ruled out that effects might have been observed at higher concentrations than tested in the FELS test. For the purpose of chronic toxicity assessment a long-term test with early life stages is strongly prefered over a prolonged acute test. However, the two studies did not overlap in test concentration, so the true level of toxicity to fish over the long-term is unclear. Overall, the long-term NOEC for fish is assumed to be around 4-6 µg/L. The prolonged acute toxicity test submitted after the Public Consultation gives results of the same magnitude as the one presented in the CLH Report.

A reliable 21 day reproduction study with *Daphnia magna* using a flow-through system with no head space was carried out. The D4 tested was > 99 % pure and stock solutions of the substance were prepared by slow-stirring dilution water with a floating layer (approximately 6 mm thick) of D4. This method of stock-solution preparation gives reproducible results and can achieve a maximum concentration of ca. 15 µg/L in hard freshwater. Five exposure concentrations were used (measured concentrations were 1.7, 1.8, 4.2, 7.9, and 15 µg/L). This study showed a statistically significant reduction in the survival at the highest concentration tested (survival in the 15 µg/L was 77 %) compared with the control population (survival was 93 %) after 21 days. The 21-day $NOEC_{survival}$ was therefore 7.9 µg/L. For the reproduction endpoint, the mean cumulative number of offspring per female daphnid was 111 in the control, 107, 92, 123, 151, and 167 in the 1.7, 1.8, 4.2, 7.9 and 15 µg/L treatment groups, respectively. There were no statistically significant differences between the control response and the treatment response in the 1.7, 1.8, and 4.2 µg/L groups, but the mean cumulative number of offspring per female was significantly higher in the 7.9 µg/L treatment group than in the control groups (the data for the 15 µg/L treatment group were not included in the statistical analysis as a reduction in daphnid survival occurred in this group). Therefore, it was concluded that concentrations of D4 ≤ 7.9 µg/L do not adversely affect the reproduction of *Daphnia magna*.

As described above, there was one toxicity study with algae available. As it is a limit test, the validity of the study was restricted. The resulting NOEC is > 6 µg/L (mean measured) (corresponding to 22 µg/L initially measured). During the Public Consultation, industry

informed that they had re-calculated the result to a scientifically more precise E_rC_{10} of > 22 µg/L (initial measured) (the maximum water solubility level in the test medium).

For the long-term (chronic) aquatic hazard, the Dossier Submitter concluded that the lowest chronic toxicity values are 14 d NOEC = 0.0044 mg/L for fish, 21d NOEC = 0.0079 mg/L for invertebrates and 96 h NOE_rC < 0.022 mg/L for algae.

The Dossier Submitter proposed to classify D4 as Aquatic Chronic 1; H410 based on high potential for bioaccumulation, no rapid degradation and a 21d NOEC for Daphnia = 0.0079 mg/L supported by a 14 d $NOEC_{fish}$ = 0.0044 mg/L. An M-factor of 10 was also proposed because the lowest NOEC value is in the range 0.01 < NOEC ≤ 0.001 and the substance is not rapidly degradable.

Comments received during public consultation

Sixteen comments were received during the Public Consultation (PC). Three Member States supported the Dossier Submitter proposal to modify the D4 classification to Aquatic Chronic 1, M-factor = 10. In addition, comments were provided by individuals (UK, US and Canada). One company and two industry associations also gave comments. 'Reconsile REACH Consortium' informed that they had changed the self-classification of D4 to a weight of evidence Aquatic Chronic 2 classification based on chronic NOECs ≥ 15 µg/L and rapid degradability or high bioaccumulation potential. This classification was supported by another industry organisation.

Physical-chemical properties and degradation

It was indicated by Industry, that test criteria and procedures developed for hydrocarbon-based chemicals are not appropriate to use for D4 due to its low water solubility, relatively high vapour pressure, very high Henry's law constant and high Log K_{ow}. Air is the final compartment of residence in the environment. Environmental exposures to D4 were expected to be minimal due to the lack of reliable evidence that D4 in air could be re-deposited into soil or water or absorbed by biota. This is also due to D4 having a relatively short half-life in air through degradation by hydroxyl radicals to silanols, which are not of toxicological concern. Both the very low solubility of D4 in water (56 µg/L) and its lower solubility in test media likely compromised the results of the hydrolysis and the ready biodegradation tests. Given that the recommended concentration of 10 mg D4/L in OECD TG 310 exceeded the maximum solubility of D4 more that 170-fold, the bioavailability of undissolved material is questionable. The Log K_{ow} and BCF values used to evaluate bioaccumulation were not contested by Industry.

The DS agreed that the test concentrations in degradation studies were well above the water solubility but a sediment simulation study supports the conclusion that the substance is not rapidly degradable. The DS agreed to the fact that substances with a low water solubility show a different solubility in the test media than in the water solubility test.

Hydrolysis

Comments were made related to the abiotic hydrolysis of D4 in water which is seen as a key degradation process in the environment. Both the rate of hydrolysis of D4 and

intermediates are considered as a function of pH and temperature. The siloxanediol intermediates are not expected to require classification based on their own rapid hydrolysis and the hydrolysis product DMSD is not toxic to aquatic organisms, therefore not fulfilling the criteria for classification as hazardous to the aquatic environment. Thus, D4 meets the 16 day criterion for rapid degradability. It was argued that temperature correction for the OECD TG 111 hydrolysis test data is risk assessment rather than hazard assessment and should not be used in classification. By correcting for the mean temperature of European surface waters of 12 °C and the respective median pH value of 7.94 the hydrolysis half-life of D4 is far below 16 days. Another comment argued that when correcting to 12 °C, the slight excess of the threshold of 16 days (half-life 16.7 days at pH 7) should not be considered as being specific concern, as the study report noted that the reported hydrolysis rate constants based on linear regression analysis of the earlier time points probably underestimate the actual rate by at least 10 %. Two comments referred to Annex 9 of GHS (UN, 2013; A9.4.1.1) and Annex II of the CLP Guidance (ECHA, 2015) which suggest that classification of substances should be based on consideration of both intrinsic properties of the substance and the prevailing environmental conditions, including pH and temperature.

The DS agreed that both the relevant temperature and pH values should be considered. The DS presented a study were the pH varies from 7.0 to 8.5 and can be considered as representative for Europe. D4 should be considered as not rapidly degradable because at this pH range at 12 °C, the half-life ≤ 16.7 days.

Aquatic toxicity

In many comments ecotoxicity tests were claimed not to be realistic because of using sealed exposure systems.

The DS responded that it is recommended in the CLP Guidance, in the OECD test guidelines and in the OECD Guidance No. 23 to minimise losses from test systems.

Toxicity to algae

There were also comments regarding the algae test. As it is a limit test, the validity of the study for use in chronic classification was questioned. Growth in controls was reduced similarly to that of the treated flask (one treatment level at the functional solubility of 22 µg/L). Cell density essentially remained unchanged in all flasks suggesting that D4 is not acutely toxic to the algae. The NOEC for algae > 22 µg/L (initial measured, 6 µg/L as mean measured) was based on yield/biomass but arguments were provided that OECD TG 201 and the CLP Guidance clearly indicate that the growth rate is preferred. As raw data had been reported in the study report, a re-analysis had been conducted revealing an inhibition of the average specific growth rate in the treatment group by less than 7 % after 72 h and 96 h, respectively, compared to the control. Therefore, the E_rC_{10} > 22 µg/L (initial measured), the maximum water solubility level in the test medium.

The DS agreed and informed that the study record reported only mean cell densities but not the cell counts per replicate and that recalculation was therefore not possible.

Chronic toxicity studies

Comments were made related to the fact that the stock test media were prepared at ambient temperatures in the most reliable long term studies although the test itself had been performed in colder temperature. The stock concentration, whether prepared by

slow stirring or via solvent addition methods, was typically at saturation around 25 µg/L. The slow-stiring method to produce solutions used an excess of substance and the possibility for particulates to 'break off' and be present in the media could not be excluded. The use of solvent addition could also produce over-saturation in the vicinity of the added concentrate. The stock was then taken to a test system operating at the lower temperature of around 12 °C, and used in flow through systems with dilution. It could be anticipated that the solubility of D4 would be significantly lower at 12 °C than it was under standard conditions. However, there is no information on the solubility in the test system at 12 °C. Therefore, it was possible that the aqueous media had (before dilution) an amount of substance present that exceeded the saturated solubility at the test temperature. The analytical methods used would have analysed all the D4 present, whether dissolved or undissolved. Through a personal communication with the study director of the 14 d prolonged acute toxicity study with fish, it was confirmed that the stock solution was prepared at room temperature whereas the test solution temperature was 12 °C. It was thought possible that a super-saturated solution was active during the study leading to mortality not relevant for classification.

The Dossier Submitter noted that the test media were prepared according to the OECD guidance and the test concentrations were analytically confirmed. There was no indication of any undissolved material. The measured concentration was lower than the maximum water solubility in the standard OECD TG which is not unusual. Taking the results from the tests and also the measured concentrations together, the tests were considered conclusive by the DS. Concerning the prolonged acute toxicity fish study (Anonymous, 1995), the DS was of the opinion that the proposed effect of the decrease in temperature is conjecture. During the analytical confirmation of the test concentration, nothing unusual was seen.

Daphnia study (Sousa et al., 1995)

Comments were made suggesting that the reproduction endpoint should be preferred to the mortality endpoint in the chronic *Daphnia* study (Sousa *et al*., 1995), OECD TG 211). A statistically significant difference in reproduction ($p \leq 0.05$) observed at the 7.9 µg/L compared to the control was not an actual effect since the number of offspring per daphnid did not decrease depending on the concentration (15 µg/L), but increased cumulatively from 111 (control) to 167 (15 µg/L) offspring/daphnid. A significant difference ($p \leq 0.05$) was also observed in the survival rate at the 7.9 µg/L treatment level in comparison with the control. The survival rate of parent daphnia changed from 93 % in the controls to 87 % and 77 % respectively at 7.9 µg/L and 15 µg/L. Some variability must also be noted; from two replicates used for statistical analysis only one was affected at 15 µg/L - a slight reduction in survival, and ultimately D4 exposure at 15 µg/L did not affect *Daphnia* reproduction or neonate size. Therefore, the overall chronic daphnia NOEC in this study should be considered ≥ 15 µg/L.

The DS stated that in the OECD TG 211, the survival of adults is also an endpoint to be documented as well as reproduction. In the same Guideline it is stated that parental mortality can also be used as an effect and that if parental mortality occurs in exposed replicates, it should be considered whether or not the mortality follows a concentration-response pattern. As the mortality occurred at the highest test concentration this could not be excluded. Therefore, the NOEC for long-term toxicity to *Daphnia* is taken as 7.9 µg/L.

Fish studies

Narcotic mode of action

The comments state that it was not surprising that D4 has no toxicity or has a low level of toxicity in most aquatic species. Like most hydrophobic chemicals, D4 acts via a narcotic mode of action, which requires the accumulation of chemical in the tissues to achieve a critical (toxic) body burden. Thus, the concepts of narcotic mode of action and chemical activity explain the apparent lack of toxicity of D4 to water column species under environmentally realistic conditions.

Some comments were made related to the results of a 14 day prolonged acute *Oncorhynchus mykiss* study, with an acute NOEC for mortality of 4.4 µg/L in support of the chronic hazard classification. The results of a 93 day early life-stage (ELS) study with *Oncorhynchus mykiss* had no effects up to the highest dose tested of 4.4 µg/L. Given the apparent inconsistency between the results of these two studies modelling was employed to determine the critical body burden (CBB) defined as the lowest body concentration of a chemical in an organism associated with adverse toxic effects. No adverse effects on embryos and larvae were noted when a 93 day trout ELS study was conducted at 12 °C up to the highest tested dose of 4.4 µg/L. These results are consistent with the results of the Mackay *et al*. (2015) simulation of the exposure, where fish averaged 1.6 g in weight by the end of the study. Additionally to 4.4 µg/L, five dose regimes were modelled: 6.9, 11, 12, 22, and 27 µg/L; the last of which is the functional water solubility for D4 at 13 °C (calculated). Only at 22 and 27 µg/L would the small trout accumulate sufficient D4 by day 90 of the simulation to exceed the CBB for a narcotic mode of action of 3 mmol/kg. This suggested that concentrations of D4 up to and including 12 µg/L could have been used in the 93 day trout study without any adverse effects. The combination of fish size/dose concentration indicates that CBB will not be achieved for 9 months (269 days). The results in the 14 day D4 prolonged acute study were inconsistent with the narcotic mode of action and pharmacokinetic modelled results, which indicated that dose concentrations as high as 22 µg/L should not have produced mortality in day 14 or less.

The DS did not see the differences between the critical body burden (CBB) calculations and test result in the 93-day fish study as significant because the calculations refer to LC_{50} and the test result is expressed as a NOEC. The fish size was also different in the estimatate and the test. The DS was of the opinion that the calculation presented in the comment fits very well to the results of the prolonged acute fish toxicity study and the results of the FELS test.

Several arguments were weighed up by the DS to come to the conclusion that the differences between the Mackay *et al.* (2015) calculations and the results of the experimental study are to be expected. Most notablly that the calculations refered to LC_{50} values, whilst the experimental study referred to NOECs.

RAC agrees with the DS. Mackay *et al*. (2015) employ the conventional equation for dynamic uptake from water by respiration as it applies to standardized flow-through bioconcentrations tests. RAC is of the opinion that the Mackay *et al*. (2015) modelling does not explain the inconsistency between results of the 14 day study and the results of the 93 day study. The fish size used is 5 g and 0.42 g in modelling and in the 14 day study, respectively. In the 93 day study different life stages were exposed (fertilized

eggs, embryos, larvae and juvenile fish). In addition, the results are expressed as NOEC in the tests and the modelling refers to LC_{50}. In Fairbrother & Woodburn (2016) it is stated that "Although the early life stage *Oncorhynchus mykiss* study conducted by Sousa *et al.* (1995) lasted 93 days, the rapid growth of the larval fish likely resulted in growth dilution such that critical body residues were not achieved even at the functional water solubility concentration".

Prolonged Toxicity Test – Long-term hazard

Comments were made concerning the use of the OECD 204 to assess chronic toxicity. According to the CLP guidance, Appendix I, I.2.1.2, tests consistent with OECD Test Guideline 210 (Fish Early Life Stage), the fish life-cycle test (US EPA 850.1500), or equivalent can be used in the classification scheme. The REACH IR/CSA Guidance R.7b, R.7.8.4.1 states that tests performed according to OECD 204 (Fish, Prolonged Toxicity Test: 14-Day Study (OECD 1984)) or similar guidelines cannot be considered suitable long-term tests. Therefore, the EPA 797.1400 study is not relevant for chronic toxicity and should not be used for the evaluation of chronic aquatic toxicity.

The DS agreed that OECD 204 is not considered suitable as a long-term toxicity test as only adults are exposed and maybe sensitive life stages are missed. But the OECD 204 test with D4 showed effects and this information should be used.

Assessment and comparison with the classification criteria

Degradation

Only 3.7 % of D4 degraded in 29 days in a ready biodegradability test following OECD TG 310, indicating that the substance is not readily biodegradable. RAC agrees with the comments received under Public Consultation suggesting that test concentration in the ready biodegradation study was well above the water solubility of D4. However, the OECD TG 310 is also applicable to insoluble test substances, though good dispersion of the substance should be ensured. According to the test report that was submitted to RAC, the test vessels were placed upside down on rotary shaker tables to ensure dispersion. RAC concluded that D4 is not readily biodegradable.

The average hydrolysis half-life for D4 under OECD TG 111 was calculated to be 3.9 days at pH 7 and 25 °C. At pH 4 the half-life was 1.77 hours and at pH 9 0.902 hours at 24.6 °C. However, at pH 6.99 and 9.5 °C, the half-life was 542 hours (~ 23 days). Consequently, an estimated half-life of 16.7 days at pH 7 and 12 °C was derived for freshwater. One of the degradation products was dimethylsilanediol which has not been classified for environmental hazard in the ECHA Classification and Labelling Inventory. There is no information on the environmental hazard of other intermediates or final degradation products.

The hydrolysis of D4 is dependent on both pH and temperature. Furthermore, the longest hydrolysis half-life determined within the pH range of 4-9 that is shorter than 16 days should be considered (Guidance on the Application of the CLP Criteria (Annex II.2.3.8).

D4 is not readily biodegradable, the hydrolysis half-life is longer than 16 days in environmentally realistic conditions (CLP Regulation 4.1.2.9.2.) and there is no information on environmental hazard of all degradation products. Therefore, it cannot be demonstrated that the hydrolysis products do not fulfil the criteria for classification as

hazardous for the aquatic compartment. RAC is of the opinion that D4 is not rapidly degradable.

Bioaccumulation

The CLH report contains three fish bioconcentration (BCF) studies:

1. 28 day kinetic BCF for fish of 13 400 L/kg re-analysed to BCF of 14 900 L/kg (lipid content=6.4 %).

2. 39 day steady-state BCF for fish of 3 129 L/kg for the higher exposure level and 3 000 L/kg for the lower exposure level.

3. 46 day steady state BCF for fish was 3 329 L/kg at the higher exposure level and 3 967 L/kg at the lower. A kinetic BCF of 4 106 L/kg was estimated for the higher treatment level and 5 540 L/kg for the lower.

Based on this evidence (supported by a Log Kow value of 6.488), RAC considers that D4 has a high potential to bioaccumulate.

Toxicity

Acute

No effects were seen within the accepted solubility limit of D4 in the acute toxicity studies presented in Table 1.

Chronic

The chronic tests are presented in Table 2.

RAC agrees with the DS on using sealed exposure systems to study the toxicity of D4 for classification purposes. The test methods used for D4 follow a tiered approach for selecting an appropriate exposure system suggested in OECD 23 step 4: Closed semi-static renewal or continuous flow-through system, with or without headspace, analytically determined exposure concentrations.

In a chronic 93 day fish early life stage study, no effects were seen at the highest tested concentration of 4.4 µg/L. There are in addition two 14 day fish prolonged acute toxicity tests where effects were seen and NOECs of 4.4 and 6.8 µg/L were determined. RAC agrees with the DS's opinion that OECD TG 204 is not considered suitable as a long-term toxicity test, as only adults are exposed and sensitive life stages are missed. However, these 14 day studies with D4 showed effects and this information is useful as supportive evidence.

In a 21 day Daphnia test, a NOEC value of 7.9 µg/L was determined for survival and a NOEC greater or equal to 15 µg/L for growth and reproduction. RAC agrees to use the mortality endpoint in relation to this study. In OECD TG 211, the survival of adults is also an endpoint to be documented as well as reproduction and can be used as an endpoint.

In a 96 hour algae limit test an E_rC_{10} greater than 22 µg/L (initial measured, the limit of water solubility in the test media) was determined. The mean measured concentration of 6 µg/L as the algae E_rC_{50} is the correct interpretation of the test outcome according to RAC. Although the REACH Registration dossier states that the cell density was decreased 18% in the treatment group, cell densities in both the test and control systems were

lower than expected. An additional open-system reference control demonstrated that the restricted gaseous exchange in the sealed system caused this apparent reduction in growth rate. During the test period, cell density in the control group grew by a factor of 18 and by a factor of 16.5 after 72 h, thereby fulfilling OECD TG 201 validity criteria, despite the fact that the actual test followed an EPA Guideline. RAC agrees that E_rC_{10} is preferred to $NOEC_{biomass}$.

Comparison with the criteria

According to the Guidance on the Application of the CLP Criteria, a substance is considered to be not rapidly degradable unless at least one of the following is fulfilled:

- the substance is demonstrated to be readily degradable in a 28 day test for ready degradability,
- the substance is demonstrated to be ultimately degraded in a surface water simulation test with a half-life of < 16 days,
- the substance is demonstrated to be primarily degraded biotically or abiotically e.g. via hydrolysis, in the aquatic environment with a half-life < 16 days and it can be demonstrated that the degradation products do not fulfil the criteria for classification as hazardous to the aquatic environment.

D4 does not fulfil any of the criteria above and is, thus, considered to be not rapidly degradable.

The BCF values are greater than the classification limit of 500 and the Log K_{ow} is also greater than the classification limit of 4. Consequently, RAC agrees with the DS that D4 is considered to be bioaccumulative for classification purposes.

In the available acute toxicity studies no effects were seen and **RAC is of the opinion that no acute classification is needed for D4**.

Altogether RAC agrees with the DS. The lowest chronic toxicity value was the NOEC of 0.0079 mg/L for aquatic invertebrates. Following the criteria for long-term (chronic) hazard, D4 warrants classification as **Aquatic Chronic 1**; **H410** with an **M-factor of 10** (not rapidly degradable and chronic toxicity in range of 0.01 < NOEC ≤ 0.001).

12 EVALUATION OF ADDITIONAL HAZARDS

Not addressed in this dossier.

13 ADDITIONAL LABELLING

None

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15 ANNEXES

Annex I (confidental)