# *Executive summary of the report*
# "Does D4 meet PBT or vPvB Criteria? Regulation in the context of developments in science"

The purpose of this executive summary is to provide a short and easily read compilation of the findings of the report **"Does D5 meet PBT or vPvB Criteria? Regulation in the context of developments in science**". The aim of the report is to present a summary of the available evidence on the persistence (P), bioaccumulation (B) and toxicity (T) properties of the siloxane octamethylcyclotetrasiloxane (CAS 556-67-2), "D4". The study was carried out following the indications of D5 and D4 as vPvB and PBT respectively, as expressed by the ECHA PBT expert group and in the ECHA Member States Committee opinion adopted in April 2015.

A weight-of-evidence assessment of the available evidence of "P", "B" and "T" properties is indicated as a relevant and useful approach by the REACH regulation and guidance, and other expert sources. The current report provides a collection of the available evidence in terms of lines of inquiry and considers this evidence in the overall conclusion on each of the properties.

**Process**

The driving force behind the work presented in this report is the view that the weight-of-evidence approach allows a substance to be appraised as PBT in the light of all available lines of evidence. The criteria for "P", "T" and in particular the criterion for "B", as they are set out in REACH and associated guidance material, serve to identify substances that *could* require a precautionary approach. This approach is necessary where there is a limited evidence-base and swift regulatory action is required. However, where there is a substantial body of evidence, as in the case of D4, it is not enough to rely on indicative criteria only, real life behaviour should also be considered. The intention of the Regulation to restrict the use of hazardous substances should prevail. This should be done using robust scientific methods.

The existing evidence comprises a considerable amount of data on D4, including that which has been used for the REACH registration dossier, as summarised below.

Emerging consensus amongst environmental scientists worldwide is that current criteria alone do not allow for an accurate assessment of PBT characteristics of a substance. An international expert workshop in 2008 (Klecka et al., 2009) concluded that the existing regulatory framework for evaluating PBTs is not consistent with the latest scientific advancements.

"P", "B" and "T" are considered to be different but inter-related properties and a conclusion regarding D4 must therefore consider all three properties together. Of the three criteria, the properties of D4 in respect to the "B" criterion are subject to the most uncertainty because the "B" criterion is based on relative rather than absolute measures. It is therefore paramount that the evaluation of the "B" criterion in relation to D4 includes all available lines of evidence.

**In the context of this review, it is necessary to first define the terms associated with "B":**

- <u>Bioconcentration</u> is used to describe the concentration of a chemical in an organism derived from water uptake alone. The bioconcentration factor (BCF) is a point measure that is determined as the ratio of the chemical concentration in test organisms to the chemical concentration in water, at steady-state.
- <u>Bioaccumulation</u> describes the accumulation of contaminants in the tissue of organisms through water and food uptake. The bioaccumulation factor (BAF) is a point measure that is determined as the ratio of the chemical concentration in test organisms to that in water, at steady-state.
- <u>The biomagnification factor</u> (BMF) is the lipid-normalized ratio of the chemical concentration in the predator to the chemical concentration of the prey species. The BMF is a slope that describes the increase or decrease in concentrations of the chemical across a simple predator–prey relationship (i.e., predator and prey that are separated by a single trophic level step).

- The biota-sediment accumulation factor (BSAF) is a point measure that is determined as the ratio of the lipid-normalized biota concentration to the organic carbon-normalized sediment concentration.
- The trophic magnification factor (TMF) is similar to the BMF, in that it is a slope that expresses the average BMF across a food web. The TMF describes the increase or decrease in concentrations of the chemical in multiple organisms that occupy successively higher trophic levels or positions within a food web.

The available data with regard to the assessment of "B" for D4 comprise laboratory studies of the bioconcentration factor (BCF) and the biomagnification factor (BMF), laboratory and field studies of the biota-sediment accumulation factor (BSAF), and field studies of the trophic magnification factor (TMF).

The BCF, BAF and BSAF metrics are expressed in terms of ratios and their magnitudes therefore depend on the exposure concentrations in the tested organisms. This increases the level of variability, especially for highly lipophilic and adsorbing substances such as D4, because the outcome is dependent on the quantity of the substance in the test system. It has been shown that dual exposure (from water and diet) may have occurred in BCF and BMF studies, which may compromise the understanding of the actual exposure route (Qiao et al., 2000; Thomann, 1989).

Laboratory BCF ratios can only, to a limited extent, be applied to predict the ability of a highly lipophilic and adsorbing substance such as D4 (log $K_{OW}$ =6.5) to biomagnify in the environment. Dietary biomagnification appears to be the main route of uptake for bioaccumulation of highly lipophilic substances, as research indicates that at naturally-occurring food/water concentration ratios, uptake of highly lipophilic chemicals (i.e., log $K_{OW}$ >6) from water into biota is low compared to uptake via consumption of contaminated foodstuffs, with the importance of dietary uptake increasing with increasing lipophilicity (Thomann, 1989; Qiao et al., 2000). Uptake via water may be an important exposure route in aquatic ecosystems for lower trophic level species, but uptake from food becomes increasingly more significant as trophic position increases. Other data demonstrates that fish are able to significantly eliminate and metabolize D4 from their tissues (Domoradzki et al., 2015, a, b, c), which supports field studies (Powell et al. 2009, Powell et al. 2010, McGoldrick et al. 2014) and modelling (Kim et al. 2015) demonstrating that food web biomagnification of D4 does not occur. Field studies that demonstrate biomagnification of D4 (Borgå et al. 2012, Borgå et al. 2013, Jia et al. 2015) appear to have been strongly biased by variable exposure of food web organisms that migrate across concentration gradients in the study areas (Kim et al. 2015). Consequently, the weight of evidence of the collective information for D4 indicates that food web biomagnification of D4 does not occur in the environment.

It is difficult to clearly interpret a BCF ratio to understand biomagnification in the environment of highly lipophilc substances. Because of this, the depuration (elimination) and metabolism rates from laboratory studies (in particular, metabolism interpreted from dietary exposures) can be assessed to better predict the behaviour of D4 in the environment. Depuration rates show that elimination of D4 from fish is moderately fast (Huggett, 2015, a, b). Depuration rates from sediment organisms may be faster still (Krueger et al., 2010; Selck, 2014). Indeed, based on the collective reliable depuration rates available for D4, the use of elimination half-life as a metric for the bioaccumulation potential of chemicals, as proposed by Goss et al. (2013), indicates that D4 is not likely to bioaccumulate. There is also clear evidence of metabolism of D4 in aquatic organisms (Domoradzki et al., 2015, a, b, c); a constant metabolism rate ($k_M$) in mature fish of >0.01 $d^{-1}$ (equivalent to a half-life of <70 days). Modelling (Kim et al. 2015) demonstrates that trophic dilution of D4 (in contrast to trophic magnification) can only occur if D4 undergoes biotransformation. These findings further support the lack of biomagnification potential in the environment.

The interpretation of field TMF data available for D4 is complicated by several confounding factors, such as concentration gradients, sediment-water fugacity ratios (Fsw), organism migration, and the biotransformation rate in the ecosystem studied (Kim et al. 2015). In such complex ecosystems TMF will be biased unless these confounding factors are integrated into the TMF calculations.

A strict comparison of data with the "B" criterion as set out in Section 1 of REACH Annex XIII (using BCF data), allows for the conclusion, on the basis of BCF data alone, that D4 is vB. However, based on a review of all the lines of evidence, BCF alone is not a reliable indicator of whether the substance in reality poses a risk to the environment that could not otherwise be controlled by conventional risk assessment.

Bioaccumulation in the environment is a function of bioconcentration and biomagnification and both processes must be taken into consideration when evaluating D4 as a potential B or vB substance. If all influencing factors are considered in the assessment, there is a clear indication that D4 will not biomagnify, but will biodilute in the environment, and therefore D4 should not be considered a potential B or vB substance.

We have considered all lines of evidence in the current regulatory context and the potential concerns for bioaccumulation. Concerns are highest for lower trophic level species because direct uptake from water is most significant for organisms at lower trophic levels with bioconcentration (i.e. the BCF) being the most significant process of bioaccumulation. Under field conditions uptake from food becomes increasingly more significant as trophic position increases and dietary uptake (i.e. trophic magnification; TMF) will be the key determinant of concentration and possible toxicity in organisms that occupy higher trophic positions, such as fish. As previously discussed, D4 undergoes trophic dilution in the environment and therefore does not represent a concern to higher trophic level organisms.

- Some compounds possess a high bioconcentration factor without trophic transfer. Although water is an exposure route for lower trophic level organisms, a concern for bioaccumulation would require presence in water, high persistence in water, low potential for elimination from biota at the lower trophic levels and the potential for toxicity to these organisms. This is not the case for D4, because the substance is volatile, poorly soluble, and not highly persistent in the majority of natural waters. Its presence in surface water is low to non-existent (Knoerr, 2014), the rate of elimination from biota is moderately high and there is no demonstrated toxicity in aquatic species.

- The substance is persistent in sediment, but sediment does not give an elevated potential for uptake of the strongly-adsorbed D4 into biota. In addition to this, benthic organisms are capable of metabolism (Selck, 2014), and there is no demonstrated toxicity to these organisms (Woodburn and Powell, 2014).

In terms of the "T" criterion, D4 fulfils the criterion in terms of mammalian properties (reproduction) and long term pelagic aquatic (daphnia). However, for mammalian studies the reproductive effects measured are at high doses that, due to the physical/chemical properties of the substance, cannot be achieved in the environment. There is also no evidence of specific receptor-mediated modes of action that could suggest unexpected effects beyond what has already been characterised; the work of Redman et al. (2012) suggests that the narcotic mode of action applies for D4 with aquatic organisms. A probabilistic risk assessment with benthic organisms indicates that current field concentrations of D4, even at highly improbable distribution levels (i.e., $95^{th}$ centile), indicates virtually no overlap of D4 sediment exposures with benthic species chronic NOEC levels (Woodburn and Powell, 2014).

In addition, field information on the water residues of D4 in wastewater effluent and adjacent surface waters from Japan indicates that these water concentrations are >100-fold below the D4 chronic MATC level of 11 µg/L, based on a chronic daphnia study with D4 (Woodburn and Powell, 2014). As such, no quantifiable risk is anticipated for pelagic organisms from surface water exposure to D4 from WWTP effluent streams.

The overall conclusions on the individual parameters based on the above lines of evidence are:

**Persistence**

- The persistence (P) criteria in sediment according to Annex XIII are met, although the overall persistence (balanced across all compartments) is low.

**Bioaccumulation**

- The substance does not biomagnify in aquatic food chains.
- The substance does not biomagnify in terrestrial food chains.

**Toxicity**

- The substance fulfils the "T" criterion in terms of mammalian properties, though only in concentrations that cannot be achieved in the environment.

Conventional risk assessment would therefore be sufficient to control the risks.

**The overall conclusion is that D4 should not be considered PBT or vPvB when taking into account all lines of evidence from the robust data available.**

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