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Risk Assessment and Regulation of D5 in Canada

FUGACITY AND ACTIVITY ANALYSIS OF THE BIOACCUMULATION AND ENVIRONMENTAL RISKS OF DECAMETHYLCYCLOPENTASILOXANE (D5)

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Abstract: As part of an initiative to evaluate commercial chemicals for their effects on human and environmental health, Canada recently evaluated decamethylcyclopentasiloxane (D5; CAS no. 541-02-06), a high–volume production chemical used in many personal care products. The evaluation illustrated the challenges encountered in environmental risk assessments and the need for the development of better tools to increase the weight of evidence in environmental risk assessments. The present study presents a new risk analysis method that applies thermodynamic principles of fugacity and activity to express the results of field monitoring and laboratory bioaccumulation and toxicity studies in a comprehensive risk analysis that can support risk assessments. Fugacity and activity ratios of D5 derived from bioaccumulation measures indicate that D5 does not biomagnify in food webs, likely because of biotransformation. The fugacity and activity analysis further demonstrates that reported no-observed-effect concentrations of D5 normally cannot occur in the environment. Observed fugacities and activities in the environment are, without exception, far below those corresponding with no observed effects, in many cases by several orders of magnitude. This analysis supports the conclusion of the Canadian Board of Review and the Minister of the Environment that D5 does not pose a danger to the environment. The present study further illustrates some of the limitations of a persistence-bioaccumulation-toxicity–type criteria-based risk assessment approach and discusses the merits of the fugacity and activity approach to increase the weight of evidence and consistency in environmental risk assessments of commercial chemicals. *Environ Toxicol Chem* 2015;34:2723–2731.

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INTRODUCTION

In a comprehensive evaluation of the environmental behavior of the personal care product decamethylcyclopentasiloxane (D5; CAS no. 541-02-06) under section 64 of the Canadian Environmental protection Act [1], Health Canada concluded that the application of D5, often at high concentrations (e.g., formulations of suntan lotion can contain up to 50% D5), does not pose a danger in Canada to human life or health. In contrast, Environment Canada concluded that when D5 enters the environment, typically at low concentrations, it has or may have an immediate or long-term harmful effect on the environment [2]. The conclusion by Environment Canada was reversed by a Board of Review for Decamethylcyclopentasiloxane, which was established under section 333(1) of the Canadian Environmental Protection Act 1999 [3], and the Board of Review conclusion was accepted by the Minister of the Environment [4]. The Board of Review concluded that future uses of D5 will not pose a danger to the environment [3]. This case illustrates the challenges that can be encountered in the use and interpretation of scientific information in risk assessments. It further illustrates the need for the development of practices that can improve and expedite risk assessments of industrial chemicals. Risk assessments are being carried out for thousands of commercial chemicals around the world, and the outcomes have significant implications for human health and well-being, environmental health, and the economy.

As is common practice in regulatory risk assessments, the environmental risk assessment of D5 included a compilation of data on the environmental fate and possible effects of D5 [5]. This compilation included a variety of data on the exposure and toxicity of D5, measured under various conditions, using different methodologies, and in most cases expressed in different quantities and in different units. The use of such diverse data for a risk assessment poses a number of challenges. One such challenge is the ability to make comparisons of environmental concentrations. The fact that environmental exposure (e.g., concentrations in food, water, air, sediment, soil, and biota) and toxicity are often expressed in different quantities and units precludes a direct comparison of many exposure and toxicity measures because such a comparison can be tantamount to "comparing apples and oranges."

A second challenge is to determine and check for consistency among different scientific data. A lack of apparent comparability and internal consistency of much of the data available for a risk assessment can result in selective use of the data, where certain data are preferred by the assessor and others are ignored. A selective approach does not take full advantage of the scientific information available, introduces bias, and reduces reliability of the risk assessment by lessening the weight of evidence.

All Supplemental Data may be found in the online version of this article.

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The objective of the present study was to explore potential solutions to these challenges in the environmental risk assessment of D5. The thermodynamic principles of activity and fugacity [6,7] were applied to express toxicity and environmental concentrations on a common basis to better assess the bioaccumulation behavior and environmental risks of D5. Fugacity and activity are widely used in chemical engineering to describe transport and transformation [8] and have been used in medicine to describe the potencies of general anesthetics [9,10]. The fugacity and activity approach has also been applied to gain insights into chemical transport, bioaccumulation, and risk assessment [11–13]. Mackay and Arnot [14] have advocated the potential of fugacity and activity for conducting environmental risk assessments. The present study aims to demonstrate that the application of fugacity and activity provides some useful attributes to the environmental risk assessment of D5 and possibly that of many other commercial chemicals currently undergoing evaluations around the world.

METHODS

General methods

Chemical fugacity f (Pa) and activity a (unitless) are thermodynamic quantities defined by Lewis [6,7] to describe the nonideal dissolution of chemicals in different media. Fugacity, often referred to as the chemical's *escaping tendency*, is essentially the partial pressure of a substance in a medium and is defined as the ratio of the chemical's concentration (C; mol m^{-3}) and its fugacity capacity (Z; mol m^{-3} Pa^{-1}) in the medium in which it occurs

$$f = C/Z \tag{1}$$

Thermodynamic activity can be expressed as the ratio of the chemical's fugacity (f) and the chemical's fugacity of the pure chemical at a defined standard state (f^R), which is generally the fugacity of the pure chemical in an actual or subcooled liquid state at the system's temperature

$$a = f/f^R \tag{2}$$

Thermodynamic activity is also defined as the product of the chemical concentration (x; mol solute/mol solvent) and the activity coefficient (γ; unitless):

$$a = \gamma \times x \tag{3}$$

In dilute aqueous solutions, the activity coefficient of very hydrophobic, non-ionic liquid organic chemicals (such as D5) in water (γ_w) is approximately equal to the reciprocal of the chemical's aqueous solubility X in units of mol/mol.

$$\gamma_W = 1/X \tag{4}$$

Assuming that the activity coefficient γ_W is constant over the concentration gradient from 0 to X, it follows that the activity of a chemical can be approximated by the ratio of the chemical's concentration (x; mol mol^{-1}) and its solubility (X; mol mol^{-1}) in the medium in which it occurs. Dividing x and X by the molar volume of the solvent produces a method to approximate the activity in more conventional units of chemical concentration (C; mol m^{-3}) and solubility (S; mol m^{-3})

$$a = x/X = C/S \tag{5}$$

The activity coefficient (γ_P) of the chemical in a medium (M) other than water can be approximated by the product of the chemical activity coefficient in the water (γ_W) and the medium–water partition coefficient (K_{MW}; unitless) of the chemical between the medium and water

$$\gamma_M = K_{MW} \times \gamma_W \tag{6}$$

such that the activity of a chemical in medium (a_M) can be calculated as

$$a_M = \gamma_M \times x_M \tag{7}$$

The fugacity and activity approaches are complementary and are used for a common purpose: to better characterize the chemical's capacity for transport and transformation. The main difference between the fugacity and activity approaches lies in the selection of the reference phase, but otherwise the approaches are similar and produce the same results. The fugacity concept is best applied to chemicals that can exist in significant quantities in the gas phase, such as many neutral organic chemicals (including D5). For that reason, it has been applied with much success to study and model the behavior of nonionic hydrophobic organic chemicals in the environment [15]. The activity approach can be applied to involatile chemicals that do not readily enter the gas phase but that can dissolve in significant amounts in water and other solvents. The activity is related to the fugacity through the expression

$$a = f/P \tag{8}$$

where P is the liquid state vapor pressure. The solubility (for water) or sorption capacity (for non-aqueous media; S) and the fugacity capacity (Z) of a chemical substance for each individual medium are related as

$$S = Z \times P \tag{9}$$

The fugacity and activity approaches have useful attributes for environmental risk assessments. First, they provide methods for expressing chemical concentrations in different environmental media in terms of a common quantity (Table 1). This provides a method for comparing exposure and toxicity data expressed in different quantities and units. Second, the fugacity and activity have established limits in thermodynamics. The activity can range from 0 to its maximum value of 1, whereas the fugacity can range only from 0 to the chemical's vapor pressure (P), which provides the ceiling for a chemical's partial pressure. The maximum fugacity or activity provides a means to distinguish between reported chemical concentrations in the environment and in toxicological studies that can occur in the environment (i.e., $f \leq$ P or $a \leq 1.0$) and those that cannot occur in the environment (i.e., $f >$ P or $a > 1.0$). Activities greater than 1 or fugacities greater than the vapor pressure typically represent experimental artifacts and/or analytical error. The fugacity and activity approaches therefore provide a means to screen data for quality. Third, some modes of toxic action, such as nonpolar narcosis, can be identified by a specific chemical activity. For example, chemical activities of nonionic organic chemicals between 0.01 and 0.09 [14] tend to cause lethality through nonpolar narcosis. This provides an opportunity to conduct a basic form of risk assessment in the absence of

Table 1. Methods for the calculation of the fugacity and activity of decamethylcyclopentasiloxane (D5) in various abiotic and biotic environmental media

Medium	Fugacity f (Pa)	Activity (unitless)
Ambient water, effluent	$f = \frac{C_W}{Z_W}$ $Z_W = \frac{S_W}{P}$	$a = \frac{C_W}{S_W}$
Sediment and soil	$f = \frac{C_{OC}}{Z_{OC}}$ $Z_{OC} = K_{OC} \times Z_W$	$a = \frac{C_{OC}}{S_{OC}}$ $S_{OC} = K_{OC} \times S_W$
Invertebrates, fish, avian tissues, marine mammals, terrestrial mammals	$f = \frac{C_L}{Z_L}$ $Z_L = K_{LW} \times Z_W \approx K_{OW} \times Z_W$	$a = \frac{C_L}{S_L}$ $S_L = K_{LW} \times S_W \approx K_{OW} \times S_W$

Symbol	Description	Units
f	Fugacity	Pa
a	Activity	Unitless
C_W	Concentration in water	mol m^{-3}
C_{OC}	Concentration in organic carbon $C_{OC} = C_S \times \frac{d_{OC}}{\phi_{OC}}$	mol m^{-3}
C_L	Concentration in lipids $C_L = C_B \times \frac{d_L}{\phi_{LB}}$	mol m^{-3}
C_S	Concentration in sediments	mol $(1000\,kg)^{-1}$
C_{OC}	Concentration in organic carbon of sediments	mol $(1000\,kg)^{-1}$
C_B	Concentration in biota	mol $(1000\,kg)^{-1}$
Z_W	Fugacity capacity in water	mol Pa^{-1} m^{-3}
Z_{OC}	Fugacity capacity in organic carbon	mol Pa^{-1} m^{-3}
Z_L	Fugacity capacity in lipids	mol Pa^{-1} m^{-3}
φ_{OC}	Total organic carbon content of sediments	(1000 kg OC) (1000 kg dry wt)$^{-1}$
φ_L	Total lipid content of biota	(1000 kg lipid) (1000 kg wet wt)$^{-1}$
d_{OC}	Density of organic carbon	(1000 kg) (m^{-3})
d_L	Density of lipid	(1000 kg) (m^{-3})
L	Lipid content of biota	(1000 kg lipid) (1000 kg dry wt)$^{-1}$
S_{OC}	Sorptive capacity of organic carbon $S_{OC} = S_W \times K_{OC}$	mol m^{-3}
S_L	Sorptive capacity of lipid $S_L = S_W \times K_{LW} \approx S_W \times K_{OW}$	mol m^{-3}

toxicity data. In the present study, we applied a fugacity and activity–based risk assessment to D5, which is a neutral hydrophobic organic substance with a potential to cause nonpolar narcosis and hence is well suited for this application. However, the approach can be further extended to express other toxicity metrics and modes of toxic action in terms of activities or fugacities.

Fugacity and activity calculations

The application of the fugacity or activity concept requires that either the fugacity capacities (for the fugacity approach) or the solubilities (for the activity approach) of the chemical substance in environmental media are known or can be determined. Table 1 lists the methods used for estimating the fugacity capacities (in Pa) and solubilities (in mol m^{-3}) of D5 in media from the ambient environment where D5 concentrations have been measured and in bioaccumulation and toxicity tests. Table 2 lists the physical–chemical properties for D5 that were used to determine the fugacity capacities and solubilities. Several assumptions were made in the calculations of fugacities and the activities of D5. First, it was conservatively assumed that ambient water and effluents do not contain organic matter. The presence of organic matter increases the fugacity capacity and solubility of D5 in the effluent (or water) and decreases the fugacity and activity of D5 in the effluent (or water). Second, it was assumed that organic carbon was the predominant sorption phase of sediment and soil particles and contained the majority of the mass of D5. This assumption often is made in environmental fate studies of nonionic hydrophobic organic substances, is supported by many studies [16], and is appropriate for D5, which has a very high octanol–water partition coefficient (K_{OW}) of $10^{8.09}$ and organic carbon–water partition coefficient (K_{OC}) of $10^{5.17}$. It is noteworthy that the K_{OC} of D5 is much lower than typically would be expected from its K_{OW}. It is typical for nonionic hydrophobic organic substances (studied to date) to possess a K_{OC} that is within 14% to 87% of the K_{OW} [16]. However, the K_{OC} of D5 is only $10^{5.17}/10^{8.09}$ or 0.12% of its K_{OW}. Third, it was assumed that in biological samples, lipids were the predominant sorption phase that contained the great majority of D5 and that the solubility of D5 in lipids was approximately equal to that in octanol (i.e., the lipid–water partition coefficient [K_{LW}] was equal to K_{OW}). Seston et al. [17] have shown using Abraham solvation equations that D5 is approximately 1.4 times more soluble in storage lipids than in octanol, whereas D5 is approximately 40 times less soluble in membrane lipids than in octanol. As further detailed in the Supplemental Data (Figure S1), the log K_{LW} for D5 can be expected to be within $\pm$ 0.20 log unit error of the log K_{OW} for D5 in organisms with a lipid composition consisting of up to 59% (kg membrane lipids/kg lipids) membrane lipids. The fraction of the total amount of lipids in aquatic organisms that are membrane lipids ranges from approximately 20% for fish [18] to approximately 80% for benthic invertebrates such as chironimids [19]. Hence, in the absence of information on the membrane/storage lipid composition of the organisms considered in the present study, the fugacity and activity of D5 in biota were calculated assuming that the log K_{OW} of D5 represents the sorptive capacity of the lipids in organisms (i.e., $K_{LW} = K_{OW}$). This assumption can produce an approximately 3-fold (see Supplemental Data) underestimation of the fugacity and activity of D5 in benthic invertebrate species with a lipid composition containing a low fraction (less than approximately 20% kg

Table 2. Summary of the physical and chemical properties of decamethylcyclopentasiloxane (D5) used in the risk analysis

Property	Value used	Reference
Molecular weight (g mol^{-1})	370.77	
Molar volume (cm^3 mol^{-1})	386.5 (20 °C)	[31]
Density (kg/m^3)	970 (10 °C)	[32]
	954 (25 °C)	[32]
Melting point (°C)	−38	[33]
Boiling point (°C)	210	[33]
Vapor pressure (Pa)[a]	6.28 (10 °C)	[24]
	22.7 (23 °C)	
	60.0 (37.5 °C)	
Water solubility (mol m^{-3})		
Freshwater		
	1.5×10^{-4} (10 °C)	Estimated[b]
	4.6×10^{-5} (25 °C)	[34]
	1.9×10^{-5} (37.5 °C)	Estimated[b]
Seawater[c]		
	5.4×10^{-5} (10 °C)	
	2.1×10^{-5} (25 °C)	
	9.7×10^{-6} (37.5 °C)	
K_{OW} (unitless)[d]	$10^{7.45}$ (10 °C)	[24,35]
	$10^{8.09}$ (25 °C)	
	$10^{8.57}$ (37.5 °C)	
K_{OC} (unitless)[e]	$10^{4.53}$ (10 °C)	[23]
	$10^{5.17}$ (25 °C)	
	$10^{5.65}$ (37.5 °C)	
K_{OA} (unitless)	$10^{4.93}$ (25 °C)	[24,35,36]

[a]Vapor pressure (P) values (in units of Pa) were derived from the empirical equation for the temperature dependence of P: $\log P = 11.87 - 3135/T$, where T is temperature in Kelvin. The vapor pressure measured at 23 °C was used to represent the vapor pressure at 25 °C.
[b]The solubilities of D5 in water at nonstandard temperature were estimated using measured temperature dependence of the air–water partition coefficients and vapor pressure described in Xu et al. [24].
[c]Aqueous solubilities in seawater were calculated from the freshwater solubilities according to Xie et al. [20] as the product of the aqueous solubility of D5 in freshwater and $10^{(0.0009 \times \text{molar volume})}$.
[d]Octanol–water partition coefficients (Log K_{OW}) at different temperatures were derived from the empirical equation [24] for the temperature dependence of $\log K_{OW}$: $\log K_{OW} = 20.15 - 3596/T$, where T is temperature in Kelvin.
[e]Organic carbon–water partition coefficients (Log K_{OC}) at different temperatures were derived from the empirical $\log K_{OC}$ of 5.17 at 25 °C equation and a temperature dependence equal to that determined for octanol [24]: $\log K_{OC} = 17.23 - 3596/T$, where T is temperature in Kelvin. K_{OA} = octanol-air partition coefficient (unitless).

storage lipids/kg lipids) of storage lipids. Fourth, it was assumed that 10 °C is a reasonable estimate of the average temperature of the effluent, water, sediment, plankton, invertebrate, and fish samples collected from the locations in the northern United States and Europe. For the calculation of the activities and fugacities of D5 in avian and mammalian samples, we used a temperature of 37.5 °C. To calculate the activities and fugacities of D5 in the toxicity studies listed in Supplemental Data, Table S8, a temperature of 25 °C was selected. Vapor pressures, water solubilities, K_{OW}, and K_{OC} at temperatures of 10 °C, 25 °C, and 37.5 °C were used for the calculation of the D5 fugacities and activities. The derivation of these physical–chemical properties is detailed in Table 2. The water solubility of D5 in seawater was calculated from the solubility in freshwater according to Xie et al. [20].

Ratios of fugacities and activities

Burkhard et al. [3] have advocated the use of fugacity ratios as a method to evaluate various bioaccumulation metrics. Fugacity ratios (R) are ratios of the chemical's fugacity (or activities) in an organism (B) relative to that in its exposure medium (M; e.g., water, diet, sediment) as measured in bioaccumulation tests at steady state (f_B/f_M) or its corresponding activity ratio (a_B/a_M). A steady-state organism–medium fugacity ratio ($R = f_B/f_M$) or activity ratio ($R = a_B/a_M$) greater than 1 ($R > 1$) indicates that a substance has a tendency to biomagnify in food webs. A fugacity ratio or activity ratio equal to 1 ($R = 1$) indicates a chemical distribution according to equilibrium partitioning. A fugacity ratio or activity ratio less than 1 ($R < 1$) indicates that a chemical in organisms will be below its equilibrium concentration with the exposure medium at steady state, for example because of biotransformation and/or growth dilution. Organism–medium fugacity or activity ratios greater than 1 are of special environmental relevance because they indicate the occurrence of chemical biomagnification in the food web.

Bioconcentration factors (BCFs), biomagnification factors (BMFs) and biota–sediment accumulation factors (BSAFs) from laboratory-based bioaccumulation tests (which are summarized in the Supplemental Data, Table S1, and reviewed in more detail in accompanying papers by Fairbrother et al. [21] and Gobas et al. [22]), were expressed in terms of fugacity and activity ratios as described in Table 3. Fugacity and activity ratios for rainbow trout (*Oncorhynchus mykiss*) were derived at 10 °C, whereas the ratios for the other aquatic species were calculated at 25 °C, close to temperatures at which the experiments were conducted. Table 3 illustrates that fugacity ratios and activity ratios are affected by error in K_{LW} (which was assumed to be equal to K_{OW}) and K_{OC} but not by error in the vapor pressure or the aqueous solubility, because these properties occur both in the numerator and denominator of the ratios and hence cancel out (Table 3). The calculation of the fugacity and activity ratios for the BMF is not affected by errors in K_{OW}, K_{OC}, or vapor pressure and aqueous solubility, and the error in its value reflects only experimental error. The standard deviations of log K_{OW} and log K_{OC} can be estimated at approximately 0.2 log unit [23,24], equivalent to a factor of 1.6. The lack of an error term in the reporting of the BCF, BMF, and BSAF makes it impossible to calculate an actual error for the fugacity and activity ratios.

Ambient concentration data

Effluents. Concentrations of D5 in effluents from municipal and industrial waste water and sewage treatment plants and 1 landfill site for locations in Northern Europe, Germany, and France were compiled from various literature sources, which are summarized in Supplemental Data, Table S2, and reviewed in Mackay et al. [25]. Samples from industrial wastewater effluents were from silicone-producing facilities. The D5 concentrations in effluent varied from 0.02 μg/L to 27 μg/L. The highest concentrations were observed in effluents of wastewater treatment plants from silicone production facilities. Concentrations were expressed in terms of fugacity and activity as described in Table 1.

Ambient water. The D5 concentrations in ambient surface water were compiled from various literature sources, which are summarized in Supplemental Data, Table S3, and reviewed in the accompanying papers by Fairbrother et al. [21] and Mackay et al. [25]. The D5 concentrations in water were available only for locations in Northern Europe. The majority of water samples were collected downstream of wastewater or sewage treatment plants and do not represent concentrations in environments remote from sources. Concentrations varied from the method detection limit (ranging between 0.01 μg/L and 0.07 μg/L) to 0.151 μg/L. Approximately 65% of documented D5 concentrations in water

Table 3. Methods for the calculation of fugacity and activity ratios from various bioaccumulation metrics[a]

Bioaccumulation metric	Fugacity ratio	Activity ratio
$BCF = \frac{C_B}{C_W}$	$R = \frac{f_B}{f_W} = \frac{BCF \times d_L \times Z_W}{\varphi_L \times Z_L}$ $Z_W = \frac{S_W}{P}$ $Z_L = K_{LW} \times Z_W \approx K_{OW} \times Z_W$	$R = \frac{a_B}{a_W} = \frac{BCF \times d_L \times S_W}{\varphi_L \times S_L}$ $S_L = K_{LW} \times S_W \approx K_{OW} \times S_W$
$BMF = \frac{C_B}{C_D}$	$R = \frac{f_B}{f_D} = \frac{BMF \times \varphi_{LD}}{\varphi_{LB}}$	$R = \frac{a_B}{a_D} = \frac{BMF \times \varphi_{LD}}{\varphi_{LB}}$
$BSAF = \frac{C_B}{C_S}$	$R = \frac{f_B}{f_S} = \frac{BSAF \times \varphi_{OC} \times d_L \times Z_{OC}}{L_B \times d_{OC} \times Z_L}$ $Z_L = K_{LW} \times Z_W \approx K_{OW} \times Z_W$ $Z_{oc} = K_{oc} \times Z_w$	$R = \frac{a_B}{a_S} = \frac{BSAF \times \varphi_{OC} \times d_L \times S_{OC}}{L_B \times d_{OC} \times S_L}$ $S_L = K_{LW} \times S_W \approx K_{OW} \times S_W$ $S_{oc} = K_{oc} \times S_w$

Symbol	Description	Units
f	Fugacity in biota (f_B), diet (f_D), water (f_W), or sediment (f_S)	Pa
a	Activity in biota (a_B), diet (a_D), water (a_W), or sediment (a_S)	Unitless
BCF	Bioconcentration factor	L (kg organism wet wt)$^{-1}$
BMF	Biomagnification factor	kg diet wet wt (kg organism wet wt)$^{-1}$
$BSAF$	Biota sediment accumulation factor	kg sediment dry wt (kg organism wet wt)$^{-1}$
C_D	Concentration in diet	mol (1000 kg wet wt)$^{-1}$
Φ_{LD}	Lipid content of biota diet	(1000 kg lipid) (1000 kg wet wt)$^{-1}$

[a]The metrics are the bioconcentration factor (BCF), the laboratory-derived biomagnification factor (BMF), and the biota–sediment accumulation factor (BSAF).
[b]For definitions of other terms used in the calculations, see Table 1.

were below the method detection limit. For the risk assessment, it was conservatively assumed that concentrations determined to be below the method detection limit were equal to the method detection limit. Also, it was conservatively assumed that the water does not contain organic particulate matter, which reduces the fugacity and activity in the water. Because the water was collected from locations in northern Europe and water temperatures were not always stated, an average temperature of 10 °C was assumed.

Sediments. The D5 concentrations in ambient surface sediments were compiled from various literature sources, which are summarized in Supplemental Data, Table S4, and reviewed in the accompanying papers by Fairbrother et al. [21] and Mackay et al. [25]. The D5 concentrations in sediments were only available for Canada, Norway, and the United States. They include both freshwater and marine sediments. Concentrations varied between 0.004 μg/g and 0.79 μg/g dry weight of sediment. Total organic carbon contents (kg organic carbon/kg sediment dry wt) were available for all sediment samples and varied between 2.1% and 5.1%.

Invertebrates. Reported D5 concentrations in plankton and a range of freshwater and marine invertebrate species from Northern Europe and the United States were compiled from various literature sources, which are summarized in Supplemental Data, Table S5, and reviewed by Fairbrother et al. [21]. Samples included both whole-body single and composite samples. Lipid contents (kg lipid/kg fish wet wt) varied from 0.3% to 7% (Supplemental Data, Table S5), and D5 concentrations varied from 0.0004 μg/g to 0.55 μg/g wet weight.

Fish. Reported D5 concentrations in various freshwater and marine fish species from Northern Europe, Canada, and the United States were compiled from various literature sources, which are summarized in Supplemental Data, Table S6, and reviewed by Fairbrother et al. [21]. Fish samples included whole body, composite, and specific tissue samples. For all fish samples, a lipid content was reported, which varied from 0.9% to 39% (Supplemental Data, Table S6). The D5 concentrations varied from 0.0014 μg/g to 1.7 μg/g wet weight.

Birds and mammals. Limited numbers of D5 concentrations were reported in eggs, liver, and muscle tissues of several avian species and in cetacean blubber samples from northwestern Europe together with the sample lipid contents (Supplemental Data, Table S7). In addition, a few samples of fish-eating mink from Lake Pepin in the United States have been analyzed for D5, and the reported concentrations and associated lipid contents are given in Supplemental Data, Table S7.

Toxicity data

Available toxicity data for D5 have been compiled, reviewed, and discussed in Fairbrother et al. [21]. That study shows that there are no reported concentrations associated with observed toxic effects of D5 in any medium. It also summarizes no-observed-effect concentrations (NOECs) for D5 of 62 μg/g to 641 μg/g dry weight for survival and growth of a freshwater amphipod (*Hyalella azteca*) at 25 °C, between 69 μg/g and 70 μg/g dry weight for male development and development rate of a midge (*Chironomus riparius*), and between 336 μg/g and 1272 μg/g dry weight for survival and reproduction of a freshwater oligochaete (*Lumbriculus variegatus*; Supplemental Data, Table S8). Because the organic carbon content of the sediments were also reported, it is possible to calculate the fugacity and activity of D5 for the concentrations at which no effects were observed (Supplemental Data, Table S8). Fairbrother et al. [21] further summarized the NOECs for effects on productivity for earthworms (*Eisenia andrei*) of 507 μg/g dry weight; for impacts on root dry mass for barley (*Hordeum vulgare*) of 77 μg/g dry weight soil, and for effects on survival of springtails (*Folsomia candida*) of 377 μg/g dry weight (Supplemental Data, Table S8). The organic carbon content of the soils was not reported and was assumed to be 3%, typical for Organisation for Economic Co-operation and Development artificial soils [21]. The toxicity data were converted to fugacity and activity as described in Table 1, such that they can be used for comparison to all available environmental concentration data, not only sediment or soil concentrations.

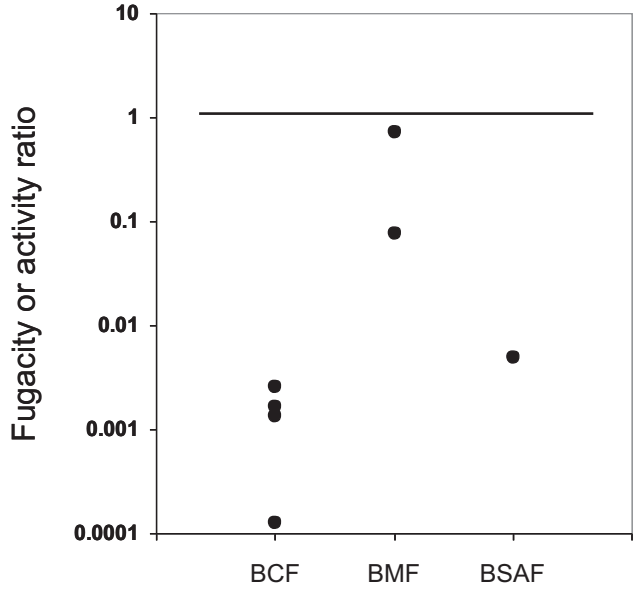

Figure 1. Fugacity or activity ratios (*y*-axis) of decamethylcyclopentasiloxane (D5) between fish and water, calculated from experimental laboratory-based bioconcentration factors (BCFs; Supplemental Data, Table S1); fish and fish diet, calculated from experimental laboratory-based dietary biomagnification factors (BMFs; Supplemental Data, Table S1); and benthic invertebrate and sediment, calculated from experimental laboratory-based biota-sediment accumulation factors (BSAFs; Supplemental Data, Table S1). The solid line represents the equilibrium ratio of 1.

RESULTS AND DISCUSSION

Figure 1 illustrates that fugacity and activity ratios for D5 derived from laboratory-based bioaccumulation studies are all less than 1 (Figure 1) and, in all but 1 case, by more than an order of magnitude. We therefore conclude that fugacity and activity ratios of D5 are likely below 1, suggesting that D5 does not have a propensity to biomagnify in food webs. This observation is in agreement with several food web bioaccumulation field studies, which report trophic dilution of D5 in aquatic food webs and trophic magnification factors for D5 of less than 1 [22]. Only studies in Lake Mjøsa, Norway [26,27] have indicated biomagnification, as discussed in more detail in Gobas et al. [22].

The use of fugacity and activity ratios can also help to improve data consistency. For example, the combination of a high BSAF of D5 in *L. variegatus* (4.29 kg dry wt/kg wet wt), low trophic magnification factors ($\leq$1.0 in all but 1 food web [range, 0.2–3.2]), and intermediate BCFs values (range, 1120–13 300 L/kg wet wt) provides inconsistent signals about the bioaccumulation behavior of D5. In contrast, the fugacity and activity ratios provide a more consistent view of D5 bioaccumulation. This view includes bioconcentration to levels below equilibrium values and a lack of dietary biomagnification in all studies except that in Lake Mjøsa, likely as a result of the biotransformation of D5 in aquatic organisms, and biotransformation and respiratory loss of D5 in terrestrial organisms, both of which have been demonstrated in laboratory and modeling studies [28–30].

Figures 2 and 3 illustrate all available D5 ambient concentration data (Supplemental Data, Tables S2–S7) in relation to available toxicity data (Supplemental Data, Table S8)

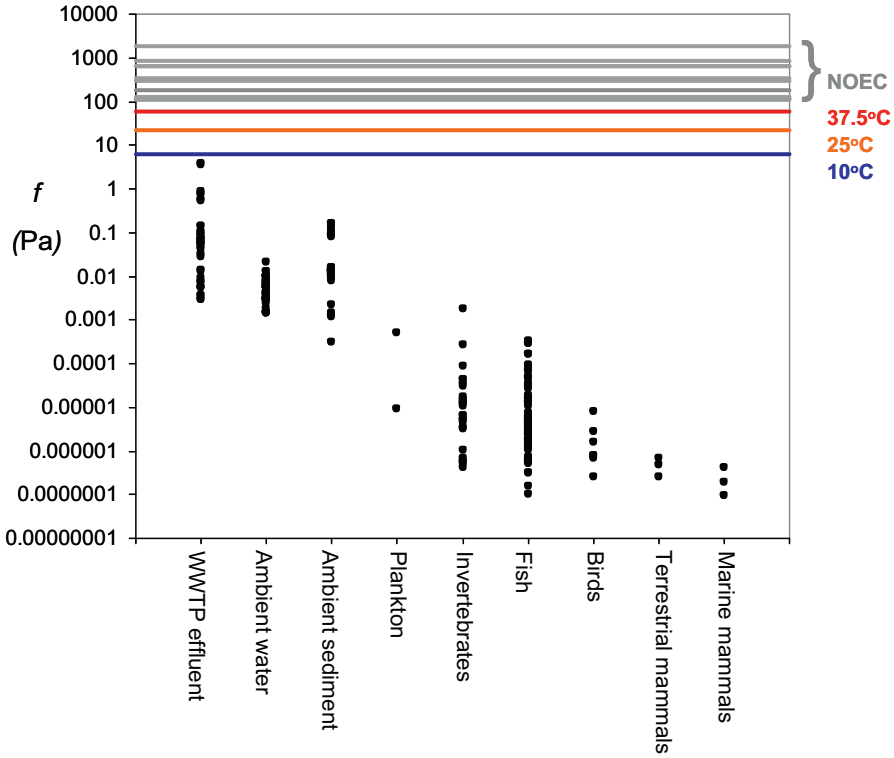

Figure 2. Decamethylcyclopentasiloxane (D5) fugacities (Pa) in wastewater treatment plant (WWTP) effluents, ambient water, ambient sediment, plankton, invertebrates, fish, birds, terrestrial mammals, and marine mammals from different locations in the Northern hemisphere (Supplemental Data, Tables S2–S7; black filled circles) in relation to the vapor pressure at 10 °C (blue line), 25 °C (orange line), and 37.5 °C (red line; Table 1), and various no-observed-effect concentrations (NOECs; Supplemental Data, Table S8) in sediment and soil-dwelling invertebrate and plant species at 25 °C (gray lines).

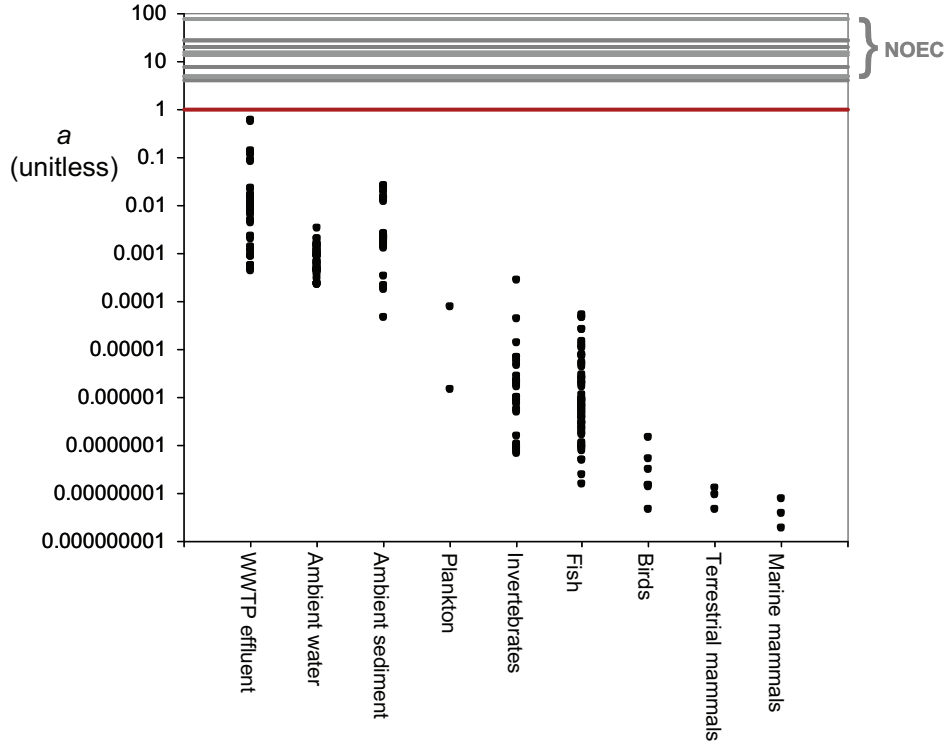

Figure 3. Decamethylcyclopentasiloxane (D5) activities (unitless) in wastewater treatment plant (WWTP) effluents, ambient water, ambient sediment, plankton, invertebrates, fish, birds, terrestrial mammals, and marine mammals from different locations in the Northern hemisphere (Supplemental Data, Tables S2–S7; black filled circles) in relation to the maximum activity (a = 1, red line) and various no-observed-effect concentrations (NOECs; Supplemental Data, Table S8) in sediment and soil-dwelling invertebrate and plant species at 25 °C (gray lines).

in a single fugacity (Figure 2) and a corresponding activity plot (Figure 3). Because the ambient data were collected from various sources and locations and at different times, it is important not to overinterpret the data. Also, the toxicity data depicted in the plot do not, in most cases, apply to the same species of organisms for which concentration data were available. Despite these limitations, however, some useful conclusions can be made.

First, all ambient fugacities (Figure 2) are less than the vapor pressure of D5 (range, 6.28–60 Pa depending on temperature), and all activities (Figure 3) are less than 1. This suggests that all reported ambient D5 concentration data are thermodynamically feasible; that is, they can exist in the environment. The highest D5 fugacities and activities were observed in effluents of wastewater treatment facilities of D5 production units. Much lower fugacities were observed in effluents of municipal wastewater treatment facilities. The D5 fugacities and activities in ambient water correspond to concentrations below or near the detection limit of 0.01 μg/L to 0.07 μg/L (i.e., fugacities of 0.0013–0.0099 Pa, or activities of 0.00023–0.0016). Because the detection limit was used as a conservative estimate of concentrations below the detection limit, it is likely that the range of D5 fugacities and activities extends to lower values than those displayed in Figures 2 and 3. The D5 fugacities and activities in ambient sediments vary between 0.00030 Pa and 0.17 Pa and 0.000047 to 0.026, respectively, and appear to be in the same range as fugacities and activities in ambient water. Fugacities and activities in biota are in general much lower than those in water and sediment. For example, the median D5 fugacity in fish of 4.4×10^{-6} Pa and the corresponding activity of 7.0×10^{-7} are several orders of magnitude below the median fugacity of 1.3×10^{-2} Pa and activity of 2.1×10^{-3} in sediments. The lowest fugacities and activities are observed for air-breathing species such as birds, terrestrial mammals, and marine mammals. The relatively low octanol–air partition coefficient of D5 ($10^{4.93}$ at 25 °C), which favors pulmonary excretion by air-breathing species, and the high trophic level positions typically occupied by these species, which maximizes the effect of trophic dilution for significantly metabolizing substances, are likely contributing factors to the very low observed fugacities and activities of D5 in these upper trophic level organisms.

Second, Figures 2 and 3 illustrate that all reported NOECs correspond to fugacities that are above the vapor pressure of D5 and activities greater than 1. This indicates that the reported NOECs were determined at concentrations above the solubility or sorption capacity of D5 in the various environmental media (i.e., sediment and soil) used to expose the test animals in the toxicity tests. This suggests that the exposure medium likely included undissolved or pure D5. Such test conditions of concentrations exceeding the solubility or sorption capacity in the exposure media are unlikely to occur in real environments, as Figures 2 and 3 illustrate. The toxicity tests are therefore not representative of possible toxicological effects for D5 in the environment. To date, there are no studies indicating that environmental concentrations of D5 can cause toxicity. This supports the Board of Review's conclusion that, based on available information, D5 does not pose a danger to the environment.

Third, in the absence of representative toxicity data, Figures 2 and 3 provide a way to assess the potential for toxicity by recognizing that for many neutral hydrophobic organic chemicals, nonpolar narcosis tends to occur at internal activities in organisms in the range 0.01 to 0.09 (unitless), which for D5 corresponds to fugacities of 0.33 Pa to 3.0 Pa at 25 °C. Nonpolar

narcosis is a basic form of toxicity that many organic chemicals appear to possess. Because D5's maximum fugacity (i.e., its vapor pressure) is 22.7 Pa at 25 °C, it is theoretically possible for D5 to cause nonpolar narcosis. However, nonpolar narcosis has not been observed or demonstrated in toxicity tests [21]. Nonpolar narcosis is also unlikely to occur in the environment, because calculated activities and corresponding fugacities in biota are several orders of magnitude below values corresponding with nonpolar narcosis (Figures 2 and 3). Biotransformation in biota is likely one of the main contributing factors to keep D5 concentrations in biota below values that can produce nonpolar narcosis.

Fourth, when the analyses presented in Figures 1 to 3—which include laboratory bioaccumulation tests, field monitoring studies, and toxicity assays in several species—are combined, an internally consistent picture emerges of the environmental fate and effects of D5 that can assist in risk assessments. In our view, D5 is a very hydrophobic substance (log $K_{OW} = 8.09$). It has a high sorption affinity for organic carbon in sediments (log $K_{OC} = 5.17$), but this sorption affinity is less than one would expect from its K_{OW} based on frequently used log K_{OW}–log K_{OC} relationships. Also, D5 has a sufficiently high affinity for air (log $K_{OA} = 4.93$), which causes a significant rate of respiratory loss in air-breathing organisms [30]. Because of the high K_{OW} of D5, the primary route of uptake of D5 in aquatic and terrestrial food webs is by dietary uptake. In aquatic and terrestrial biota, D5 is biotransformed at a rate that is sufficiently high (relative to its rate of uptake) to prevent the occurrence of dietary biomagnification. It is likely that D5 is subject to trophic dilution (i.e., the opposite of biomagnification) in food webs, causing fugacities and activities to decline with increasing trophic level. Fugacities and activities of D5 in biota are not able to reach values that are associated with nonpolar narcosis or known toxic effects.

The results of the risk analysis support the conclusion of the Board of Review that D5 is not toxic under the definition of the Canadian Environmental Protection Act [1]. According to the Act, "a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity." The present risk analysis based on fugacity and activity considerations is in agreement with traditional risk assessment methods [21] and shows that there currently is no evidence to indicate that D5 has an immediate or long-term harmful effect on the environment or its biological diversity. The analysis also provides some insights into whether D5 may cause future concerns (e.g., because of increasing production volumes or use of D5), which is emphasized in the Board of Review's conclusions. The Board of Review [3] concluded that "… based on the information before it, the projected future uses of siloxane D5 will not pose a danger to the environment." The fugacity and activity analysis shows that in the hypothetical case where the thermodynamic activity of D5 in the abiotic environment (i.e., water, sediment, soil) is at its maximum value of 1, the activities of D5 in biota can be expected to be less than those currently associated with nonpolar narcosis, because the D5 biota/water and biota/sediment activity ratios are less than 0.01 (Figure 1) and dietary biomagnification factors are also less than 1. This means that nonpolar narcosis likely cannot be achieved in most biota even at the highest possible environmental concentrations. Toxicity studies carried out to date have confirmed this. The exception may be for organisms that cannot metabolize D5. Hence, a risk analysis based on fugacity and activity considerations supports the Board's conclusions with respect to nonpolar narcosis. However, it is possible that future studies may reveal significant biological effects within the range of environmentally achievable fugacities and activities in biota. Hence, the potential of future effects cannot be completely ruled out. However, the fact that D5 apparently does not cause nonpolar narcosis at the the maximum possible concentrations in exposure media can only be viewed as a favorable environmental attribute that many other chemicals currently in commerce may not have. In a larger context, D5 exemplifies the fact that hydrophobic substances with a high K_{OW} and low aqueous solubility are not necessarily hazardous but can be safe to use. A simplistic criteria-based or bright line risk assessment approach, which uses fixed values for K_{OW}, BCF, persistence, and inherent toxicity, may not always correctly capture the actual environmental risks of chemical substances and may lead to conclusions that are in stark contrast with the reality of exposures and effects. Although we recognize that fugacity and activity are currently not part of the vocabulary of most environmental risk assessors, we also submit that the fugacity and activity approach can be a very useful tool in conducting risk assessments of many commercial chemicals.

SUPPLEMENTAL DATA

Tables S1–S8.
Figure S1. (427 KB DOC).

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Data availability—Copies of reports are available by request from the Silicones Environmental, Health, and Safety Center (SEHSC), a sector group of the American Chemistry Council (ACC). Send requests to tracy_guerrero@americanchemistry.com.

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