Environment International 62 (2014) 86–94

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Concentrations of cyclic volatile methylsiloxanes in European cosmetics and personal care products: Prerequisite for human and environmental exposure assessment

Tatsiana Dudzina [a], Natalie von Goetz [a,*], Christian Bogdal [a], Jacqueline W.H. Biesterbos [b], Konrad Hungerbühler [a]

[a] Institute for Chemical and Bioengineering, ETH Zurich, 10 Wolfgang Pauli Strasse, 8093 Zurich, Switzerland
[b] Radboud University Medical Centre, Department for Health Evidence (133), P.O. Box 9101, 6500 HB Nijmegen, The Netherlands

ARTICLE INFO

Article history:
Received 3 July 2013
Accepted 5 October 2013
Available online 31 October 2013

Keywords:
Cyclic siloxanes
cVMSs
Cyclomethicone
Concentrations
Cosmetics and personal care products

ABSTRACT

Low molecular weight cyclic volatile methylsiloxanes (cVMSs) are widely employed as emollients and carrier solvents in personal care formulations in order to acquire desired performance benefits owing to their distinctive physicochemical properties. Under current European legislation cosmetic ingredients such as cVMSs are required to be labeled on the product package only qualitatively, while for the assessment of environmental and consumer exposure quantitative information is needed. The aim of this study was therefore to measure concentrations of three cVMSs, namely octamethylcyclotetrasiloxane (D4), decamethylcyclopentasiloxane (D5) and dodecamethylcyclohexasiloxane (D6) in 51 cosmetics and personal care products (C&PCPs) that are currently available on the European market. The list of selected articles comprised a variety of hair and sun care products, skin creams and lotions, deodorants including antiperspirants, liquid foundations and a toothpaste. The target compounds were extracted from the products with different organic solvents dependent on the product matrix, followed by gas chromatography analysis with flame ionization detection (GC–FID). D5 was the predominant cVMS with the highest mean and median concentrations in all the C&PCP categories. The median concentrations of D5, D6 and D4 were 142, 2.3 and 0.053 mg/g in deodorants/antiperspirants (n = 11); 44.6, 30.0 mg/g and below the limit of quantification (<LOQ; LOQ for D4 = 0.00071 mg/g) in cosmetics (n = 5); 8.4, 0.32 mg/g and <LOQ in skin care (n = 16); 9.6, 0.18 and 0.0055 mg/g in hair care (n = 10); and, 34.8, 0.53 and 0.0085 mg/g in sun care (n = 8) products, respectively. The calculated median aggregate daily dermal exposure to D4 and D5 from multiple C&PCPs was approximately 100 times lower than the current NOAEL derived from chronic inhalation rat studies.

1. Introduction

Octamethylcyclotetrasiloxane (D4), decamethylcyclopentasiloxane (D5) and dodecamethylcyclohexasiloxane (D6) are low molecular weight cyclic volatile methylsiloxanes (cVMSs) (short name: cyclosiloxanes) consisting of four, five and six –Si–O– structural units, respectively, which are arranged in a ring with two methyl groups attached to each silicon atom. In pure form cVMSs are colorless and odorless fluids. Either as single substances or as mixtures (e.g., referred to as cyclomethicone) they are extensively being used as carrier solvents and emollients in cosmetics and personal care product (C&PCP) formulations. Applications of cVMSs stem from their distinct physicochemical properties such as high vapor pressure, low surface tension, and a high degree of compatibility with many formulation ingredients. Manufacturers began incorporating silicone materials into cosmetics and grooming products in the late 1940s. However, it was not until the 1970s, when the U.S. consumer market of cVMS containing products grew rapidly (Goddard and Gruber, 1999). Since then cVMSs have become the basic ingredients in most personal care formulations, such as deodorants, hair care and skin care products.

According to the data provided by the Skin Deep Database, which encompasses more than 75,000 C&PCPs, over 16% of cosmetics and personal care products nowadays contain cVMSs, with D5 appearing to be by far the most widely used compound (EWG, 2012). Both D5 and D6 have been recognized as high production volume (HPV) chemicals by the Organization for Economic Cooperation and Development (OECD, 2007). According to the U.S. EPA (2002) their annual import and production in the United States of America increased by ten times in the last 25 years to more than 225,000 and 22,500 t, respectively. In Europe the amounts of D4, D5 and D6 used annually for personal care applications were estimated by the Environmental Agency of the

* Corresponding author at: Safety and Environmental Technology Group, ETH Zürich, Wolfgang-Pauli-Str. 10, CH-8093 Zürich, Switzerland. Tel.: +41 44 632 0975; fax: +41 44 632 1189.
E-mail address: natalie.von.goetz@chem.ethz.ch (N. von Goetz).

0160-4120/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.envint.2013.10.002

United Kingdom in its recent environmental risk assessment reports (UK EA, 2009a,b,c) at 579, 17,300 and 1989 t for year 2004, respectively. The total trade volume of silicones in Europe reaches 2.5 billion Euros a year (CES, 2011).

Industrial manufacturing of cVMSs as well as direct usage of cVMS-containing C&PCPs by consumers can lead to significant emissions of cVMSs into air or wastewater (Gouin et al., 2013; Maddalena et al., 2011), which in combination with their large production amounts and high mobility results in these compounds being found globally in various environmental matrices including ambient air (Buser et al., 2013; Genualdi et al., 2011; McLachlan et al., 2010; Norden, 2005; Warner et al., 2010; Yucuis et al., 2013), indoor air and dust (Tuomainen et al., 2002; Lu et al., 2010), surface and sewage water (NILU, 2007; Sparham et al., 2008; Zhang et al., 2011), biota (Kaj et al., 2005a; NILU, 2007; Norden, 2005), as well as human tissue (Flassbeck et al., 2001; Hanssen et al., 2013; Kaj et al., 2005b; Kala et al., 1997; US EPA, 1987). Consumer exposure to cVMSs primarily occurs via direct use of personal care products (Health Canada, 2008) where dermal and inhalation exposure routes play the key role in building up the systemic dose with route specific uptake rates of 0.017–0.5% and 2%, respectively (Jovanovic et al., 2008; Reddy et al., 2003, 2007, 2008). Having collected and evaluated a large number of studies relevant to persistence, bioaccumulation and toxicity (PBT) properties of D4 and D5, the ECHA PBT Expert Group (ECHA, 2012) came to the conclusion that based on the available information, D4 meets the criteria for both a 'persistent, bioaccumulative and toxic' (PBT) and a 'very persistent and very bioaccumulative' (vPvB) substance in the environment. D5 fulfills the criteria for a 'very persistent and very bioaccumulative' (vPvB) substance due to its persistence in sediment and a high bioconcentration factor in fish.

Animal studies suggest that D4 and D5 exhibit rather similar toxicity profiles and may have direct and indirect effects on human health. These effects include the induction of uterine endometrial adenocarcinomas in rats following lifetime inhalation exposure with concentrations of D4 in air of several hundred parts-per-million (ppm) that correspond to an unrealistic exposure of more than 1500 mg/kg/day (Dow Corning Corporation, 2004, 2005), the increase in liver weight after subchronic oral and inhalation exposure of 100 mg/kg/day (Burns-Naas et al., 1998, 2002; Dow Corning Corporation, 1986; Jäger and Hartmann, 1991), and the decrease in fetal weight in pregnant rats treated over one week with gavage administration of 100 mg/kg/day dose of D4 (Falany and Li, 2005). The opinion of the European Scientific Committee on Consumer Safety (SCCS) on D4 and D5 present in cosmetics and personal care products (SCCS, 2010) summarizes the information on the toxicity profiles of these compounds and establishes the following critical effect levels for the safety evaluation: for both substances a no-observed-adverse-effect level (NOAEL) of 150 ppm from chronic inhalation exposure studies in rats and a lowest-observed-adverse-effect level (LOAEL) of 100 mg/kg/day from subchronic toxicity rat studies with oral dosing. On this basis the SCCS currently considers D4 and D5 safe for humans.

Although it is known that cVMSs are used in large amounts in consumer products, which therefore represent a large source of exposure for both humans and the environment, data on product concentrations are scarce. Concentrations of cVMS in C&PCPs were reported by Horii and Kannan (2008), Wang et al. (2009), and Lu et al. (2011). Their results were obtained for the North American (USA and Canada) and Asian (China and Japan) markets, but to the best of our knowledge no such data exist for Europe. In the above-mentioned studies, measured cVMS concentrations varied significantly across and within the product categories investigated and ranged between 0.01% in body washes and toilet soaps and 70% in deodorants. Voluntary reported data from the cosmetic industry on the approximate ranges of cVMS concentrations in C&PCPs (recently published by the Cosmetic Ingredient Review (CIR) Expert Panel (Johnson et al., 2012)) support the results for the American and the Canadian markets.

The objective of the present study was to measure the concentrations of cVMSs in selected cosmetics and personal care products that are currently available on the European market and are intensively used by consumers on a daily basis. Thus, we want to provide source data as a necessary input parameter for assessing environmental and human exposure. The products were selected based on the frequency of their use by Dutch consumers, as recently assessed by a questionnaire survey (Biesterbos et al., 2013). We determined concentrations of D4, D5, and D6 in 51 selected cosmetics and personal care products sold in Europe, including deodorants/antiperspirants, hair-care, skin care, and sun care products. The presence of at least one of the cVMSs of interest in an ingredient list of a product was the main inclusion criteria of this product into the study. The collected data was subsequently used in a preliminary worst-case scenario assessment of aggregate consumer exposure for D4 and D5 followed by comparison with biomonitoring data. Furthermore, the product concentrations of cVMSs determined in this study can serve as essential input data for environmental fate modeling, environmental exposure assessment, and validation of back-calculations of cVMS emissions based on the monitoring of the environmental media (Buser et al., 2013) as well as for life-cycle assessment.

2. Material and methods

2.1. Product selection

The cosmetics and personal care products (C&PCPs) for this study were selected on the basis of preliminary results of the questionnaire-based survey that investigated the use patterns of different C&PCP categories in the Netherlands (Biesterbos et al., 2012). We included consumer products of three to five most popular brands in each product category that (1) are the most intensively used by consumers considering both its frequency and amount of application, and (2) would contribute the most to consumer exposure to cVMSs because of potentially high concentrations of these compounds. The ingredient lists of selected products were examined for cVMSs' presence. Since the questionnaire data did not include full names of the products but only brand names we inspected the whole range of product names for each brand for every C&PCP category of interest. If none of the products in a brand included any of the cVMSs on its ingredients list, the brand was not further investigated. If none of the selected brands in a product category claimed to contain cVMSs, one random sample was chosen for verification.

In total 51 C&PCPs were analyzed. Among those, 46 products were purchased in retail stores in Utrecht, the Netherlands, in March 2011; all of these products were manufactured in Western Europe with the exception of one cream-deodorant produced in Canada and two stick-deodorants made in Russia. Another five products that matched the selected Dutch products by type and brand name were bought in Zurich, Switzerland, to compare cVMS concentrations by country of sale. The Swiss products were: hair repair spray, rinse-off hair conditioner, deodorant-stick, hand cream, and body lotion. All of these five product-pairs were made in the European Union. The stick-deodorants were both produced in Germany; the other four product-pairs were produced in different European countries.

The collected products can be grouped into five product categories comprised of 16 smaller subcategories (listed in brackets with n = number of products) including hair care products (hair repair spray, n = 4; rinse-off hair conditioner, n = 5; hair fixative spray, n = 1), deodorants including antiperspirants (stick, n = 4; spray, n = 5; cream, n = 1; roller, n = 1), skin lotions (body lotion, n = 4; face cream, n = 7; hand cream, n = 5), sun care products (sunscreen cream, n = 4; sunscreen spray, n = 3; aftersun cream, n = 1) and cosmetics (liquid foundations, n = 4; lipbalm, n = 1). The last product category contained only one item (toothpaste (n = 1)). Despite of no declared cVMS content, toothpaste was included in the analysis

because of its high potential for consumer exposure (high frequency of use Biesterbos et al., 2012 and oral exposure with higher uptake rate). Full names as well as the cVMSs' presence in the ingredient list of the analyzed products are given in Table SI-1 (Supporting Information).

2.2. Reagents and standards

All solvents and reagents were of analytical grade. Analytical standards included D4 and D5 (purity > 97%; Sigma Aldrich Germany Ltd.), D6 (purity 98%; TCI Europe Ltd.), tetrakis (trimethylsiloxy)-silane (M4Q; purity 97%; Sigma Aldrich Germany Ltd.) and biphenyl (BP; purity 99%; Sigma Aldrich Germany Ltd.). Individual standard solutions of these compounds in *n*-hexane were prepared monthly and stored in air-tight glassware at 4 °C.

2.3. Chemical analysis

2.3.1. Sample preparation

Triplicate samples of each product (0.1–0.5 g) were weighed in a glass tube and spiked with 50 μL of M4Q solution (8.68 μg/μL) as an internal standard. Depending on the product type the sample extraction was slightly adapted. For skin lotions and creams the samples were first topped with 3 mL of methanol (purity ≥ 99%; Sigma Aldrich Germany Ltd.), followed by addition of 3 mL of *n*-hexane (purity > 96%; Scharlau S.L., Spain), capped and then immersed into the ultrasonic bath for 15 min to allow proper mixing. Final separation of the two solvent layers was achieved by centrifugation for 15 min at 3000 rpm. The supernatant was then transferred into a glass vial with a flat bottom. For other product categories the extraction procedure was identical, but without methanol (extraction only with 3 mL *n*-hexane).

The samples were re-extracted with *n*-hexane twice following the same steps as described above. In total 9 mL of solvent was collected and will be referred to as the 'first extract'. To confirm complete extraction of target chemicals after three extractions, selected samples (n = 30) were soaked with 5 mL of *n*-hexane overnight, followed by the same extraction procedure. This extract is referred to as the 'second extract'.

Extraction was followed by reduction of the individual extract volumes to 1–2 mL under a gentle stream of nitrogen and purification by liquid chromatography on a column filled with 0.7 g of silica gel (high purity grade, pore size, 60 Å; mesh, 230–400 μm; Sigma Aldrich Switzerland Ltd.; preconditioned with *n*-hexane) and topped with 0.1–0.2 g of sodium sulfate (purity 99%; anhydrous; Acros Organics, Belgium). Target analytes were eluted from the silica gel column with 5 mL of dichloromethane:*n*-hexane solution (1:9 v/v). Dichloromethane (purity > 98%, stabilized) was purchased from Sigma Aldrich Germany Ltd.

The eluates were concentrated again to about 0.2–0.3 mL and transferred into gas chromatography (GC) vials, followed by spiking with 45 μL of biphenyl solution (10 μg/μL) as a recovery standard (RS).

2.3.2. Analysis by gas chromatography (GC)

Cyclic siloxanes were identified and quantified using a gas chromatograph (GC; HP-6890 Series GC-System, Agilent Technologies Inc., Germany) equipped with an autosampler and a flame ionization detector (FID). The cVMSs were separated on a HP-5MS column (Agilent 19091J-133; length, 30 m; diameter, 250 μm; film thickness, 0.50 μm). GC/FID was chosen for routine analyses because of its advantages over the more commonly used method of GC/MS, like cost effectiveness and less resource consumption. By including standard mixtures in the sampling sequence and random checks with GC/MS we accounted for limitations of FID compared to GC/MS (see below).

An aliquot of 1 μL was injected in splitless mode at the following GC conditions: injection port temperature: 250 °C; inlet septum type Restek BTO; initial oven temperature 80 °C kept for 3 min; initial ramp rate 20 °C/min up to 250 °C; final ramp 5 °C/min to 295 °C, and kept at 295 °C for 10 min. The FID operated at 300 °C with constant flows of hydrogen as fuel gas (40.0 mL/min) and air as oxidant (400 mL/min). Nitrogen was used as a make-up gas (43.2 mL/min) and helium as a carrier gas (constant flow: 1.0 mL/min).

The identification of the target compounds in the product samples was routinely done by injection of a standard mixture at the beginning of each sample sequence and after every nine samples under the same chromatographic conditions and subsequent intercomparison of the retention times that had to be within ±0.3 min of the retention times obtained with the standard mixtures. The possibility of interferences of other formulation ingredients by coeluting with peaks produced by target analytes was checked with tests using spiked samples (see SI) and double checking of nine selected product samples with GC coupled to an electron ionization mass spectrometer (EI/MS) (HP-6890 Series GC-System; HP-5973, column HP-5MS; equivalent temperature program). The EI/MS operated in a full scan mode. The ions used for qualifying cVMSs were m/z 281 for D4; m/z 355 and 267 for D5; and m/z 341 and 429 for D6. The qualification of the cVMSs was based on the related mass spectrum of each compound extracted and detected in the chromatograms.

The quantification of D4, D5 and D6 was done based on an internal standard quantification procedure, using M4Q as an internal standard and biphenyl as a recovery standard to check the recovery of M4Q (see Supplementary Information for more details). With the use of M4Q as an internal standard added to the samples at the beginning of the analytical procedure, all presented data are directly corrected for recovery. The relative response factors for D4, D5, and D6 against M4Q were determined with an external standard solution.

2.4. Quality assurance

To account for high volatility of the target compounds care was taken to avoid contamination of the laboratory environment and the samples. Detergents used for washing the glassware were analytically confirmed to be free of the target compounds and the laboratory staff was advised not to apply cosmetics, deodorants or a hand cream on days of analysis. In addition, to reduce the background levels of cVMSs, siloxane-free septa in the GC vial caps and in the GC-inlet were used.

Procedural blanks (n = 11) were analyzed in parallel with the samples to check for contamination occurring during sample treatment, from the glassware and reagents. The target chemicals were detected only in two procedural blanks, namely in those that were analyzed together with deodorant-spray samples. Thus, in this case cross-contamination may have occurred. These two blanks were therefore not considered in the determination of the limit of detection (LOD) and limit of quantification (LOQ). A series of eight blank (negative) samples (i.e. samples containing no analytes but with a matrix identical to that of the average sample) were tested and the noise in the ion chromatograms was determined. The LOD was then set to the mean blank noise value plus three standard deviations (SDs) of the blank noise and was normalized to the mean sample weight of 0.4 g. This resulted in LODs for D4, D5 and D6 of 350, 328 and 353 ng/g, respectively. The LOQ was set to the value of 10 SDs above the mean blank noise level and was 715, 670, and 721 ng/g for D4, D5 and D6, respectively. Blank subtraction to correct cVMS concentrations was not performed since the blank levels were all below the limit of quantification.

After every nine samples an instrumental blank, i.e. pure n-hexane, as well as a standard mixture of target analytes were injected and analyzed to check for instrumental background, carryover, signal linearity and stability. In addition, to remove any residual material from a preceding injection the GC-column was heated and kept at 295 °C for 10 min after each sample injection. None of the solvent batches contained target compounds.

All product samples were analyzed in triplicates. Half of those samples that contained detectable amounts of cVMSs had a Relative Standard Deviation (RSD) of less than 15%. Another quarter of the samples had RSDs between 15% and 25%. The RSD values larger than 25% for the remaining triplicate samples were mainly due to the low concentrations of cVMSs present in these samples. In addition, the performance of the analytical method (reproducibility) was tested by repeated analysis of five selected samples (rinse-off hair conditioner, hair repair spray, stick-deodorant, hand cream and face cream). In each case the difference between the means in the first and the second run was less than 20%.

At the method development stage recovery efficiency tests were performed with different extraction solvents (see Section 3 of SI for details). Mean recovery of the internal standard (M4Q) from all samples that were extracted with *n*-hexane was 67.7 ± 13.9%. From those samples that were first pre-soaked with methanol the mean recovery of M4Q was 65.0 ± 9.7%. Neither of the second extracts did contain significant amounts of internal standard or target analytes: the amounts were always less than 10% of those found in the corresponding first extracts.

3. Results

3.1. Concentrations of cVMSs in cosmetics and personal care products

All samples, except for the hair fixative spray, the toothpaste and the lipbalm, contained detectable amounts of at least one of the three cVMSs studied, although D5 was the most predominant one and was contained in 47 out of 51 products. Concentrations below LOQ were set to zero for the statistical analysis (lower bound scenario of a conventional substitution method for the treatment of the left-censored data (EFSA, 2010)), because cross contamination may have occurred at low concentrations. Median cVMS concentrations for every product category were insensitive to the method of treating the non-detects (see SI). The summary statistics of D4, D5 and D6 concentrations for each product subcategory are shown in Table 1 (statistical software: R v.2.15.0). The results for more general product categories are illustrated in Fig. 1.

Both D5 and D6 were detected in higher concentrations compared to D4 in each product subcategory (Fig. 1) with D5 prevailing in almost all the products. The mean and median concentrations of D5 for all the products that contained detectable amounts are 60.5 mg/g and 25.7 mg/g, respectively. The concentrations of D6, however, are in a lower range with a mean of 7.0 mg/g and a median of 0.6 mg/g. D4 was detected at least once in every subcategory, with the exception of hand and sunscreen creams. However, its concentrations (mean = 0.18 mg/g, median = 0.011 mg/g) were always two to three orders of magnitude lower than those for D5 and D6, which suggests that in most cases it was an impurity of D5 or D6. The observed trend towards using higher order cVMSs in cosmetics and personal care products was also noted in a recent CIR report (Johnson et al., 2012).

No cVMSs were detected in those products that did not list them among the ingredients, i.e. lipbalm, hair fixative spray and toothpaste. The product category "deodorants" contained the largest amounts of cVMSs (median concentrations were 0.53 mg/g, 142 mg/g and 2.3 mg/g for D4, D5 and D6, respectively). Other product categories with high cVMS concentrations were cosmetics (median = 44.6 and 30.0 mg/g for D5 and D6, respectively), sunscreen products (median = 0.0085, 34.8 and 0.53 mg/g for D4, D5 and D6, respectively) followed by skin creams and lotions (median = 8.4 and 0.32 mg/g for D5 and D6, respectively). The hair care product category had the lowest concentrations of cVMSs, i.e. medians of 0.0055, 9.6 and 0.18 mg/g for D4, D5 and D6, respectively. Interestingly, among products considered in our study the rinse-off hair care products contained approximately an order of magnitude less cVMSs than the leave-on hair care products. It should be noted that the cosmetics category in Fig. 1 apart from liquid foundations also contains the lipbalm sample, and therefore the median concentrations for this category appear lower than if it contained only the liquid foundations (see Table 1). In addition, our results showed that one of the liquid make-up samples apart from the listed D5 contained a substantial amount of D6 (approximately 40 mg/g or 4.0% w/w), which was not listed on its label.

The cVMS concentrations in Swiss marketed products were similar to those in their Dutch counterparts in three out of five selected product-pairs (the variation of D4, D5 and D6 concentrations was less than 20%). The two mismatching articles were the body lotion and the hand cream, all labeled with D5 only. The amount of D5 in the Swiss body lotion sample was tenfold higher than in its Dutch analog, whereas the hand cream purchased in the Netherlands contained twice as much D5 as its Swiss equivalent.

Table 1
cVMS concentrations (mg/g wet weight; median, mean, and range) in cosmetics and personal care products sold in Europe per subcategory.

Product subgroup (n: number of products in the subgroup)	Statistics	Concentration, mg/g wet weight		
		D4	D5	D6
Aftersun cream (n = 1)	Median	0.017	7.2	0.022
	Mean	0.017	7.2	0.022
	Range	NA[a]	NA	NA
Body lotion (n = 4)	Median	<LOQ	15.0	0.34
	Mean	0.0036	15.1	0.90
	Range	<LOQ–0.015	2.3–28.3	<LOQ–2.9
Face cream (n = 7)	Median	<LOQ	24.7	0.58
	Mean	0.31	54.2	5.6
	Range	<LOQ–1.9	<LOQ–214	0.056–70.8
Deo antiperspirant cream (n = 1)	Median	5.0	356	5.5
	Mean	5.0	356	5.5
	Range	NA	NA	NA
Deo antiperspirant roll-on (n = 1)	Median	0.016	9.0	0.15
	Mean	0.016	9.0	0.15
	Range	NA	NA	NA
Deo antiperspirant spray (n = 5)	Median	0.021	58.3	0.96
	Mean	0.086	110	2.2
	Range	0.019–0.20	35.7–285	0.51–5.3
Deo antiperspirant stick (n = 4)	Median	0.066	187	3.1
	Mean	0.065	195	2.6
	Range	0.014–0.12	142–266	<LOQ–4.1
Fixative hair spray (n = 1)	Median	<LOQ	<LOQ	<LOQ
	Mean	<LOQ	<LOQ	<LOQ
	Range	NA	NA	NA
Hair conditioner (rinse-off) (n = 5)	Median	<LOQ	6.4	0.12
	Mean	0.0054	5.3	0.11
	Range	<LOQ–0.013	0.013–10.3	0.020–0.21
Hair repair spray (n = 4)	Median	0.056	44.8	1.2
	Mean	0.054	52.4	2.3
	Range	<LOQ–0.11	18.1–102	0.65–6.3
Hand cream (n = 5)	Median	<LOQ	1.4	<LOQ
	Mean	<LOQ	3.8	1.6
	Range	<LOQ	0.54–12.5	<LOQ–7.4
Lipbalm (n = 1)	Median	<LOQ	<LOQ	<LOQ
	Mean	<LOQ	<LOQ	<LOQ
	Range	NA	NA	NA
Liquid foundation (n = 4)	Median	0.13	96.5	34.0
	Mean	0.16	107	55.2
	Range	<LOQ–0.39	21.0–213	2.4–151
Sunscreen cream (n = 4)	Median	<LOQ	25.3	0.51
	Mean	<LOQ	30.6	4.5
	Range	<LOQ	5.4–62.8	<LOQ–14.3
Sunscreen spray (n = 3)	Median	0.033	37.4	1.8
	Mean	0.15	61.1	6.8
	Range	0.027–0.39	36.4–110	0.041–18.6
Toothpaste (n = 1)	Median	<LOQ	<LOQ	<LOQ
	Mean	<LOQ	<LOQ	<LOQ
	Range	NA	NA	NA
All products (n = 51)	Median	0.011	25.7	0.64
	Mean	0.18	60.5	7.0
	Range	<LOQ–5.0	<LOQ–356	<LOQ–151

Limits of quantification (LOQ): 0.00071 mg/g for D4; 0.00067 mg/g for D5; 0.00072 mg/g for D6. The values below LOQ were set to zero to calculate median and mean concentrations in each product subcategory.

[a] NA — not available, because the subcategory consists of a single product sample.

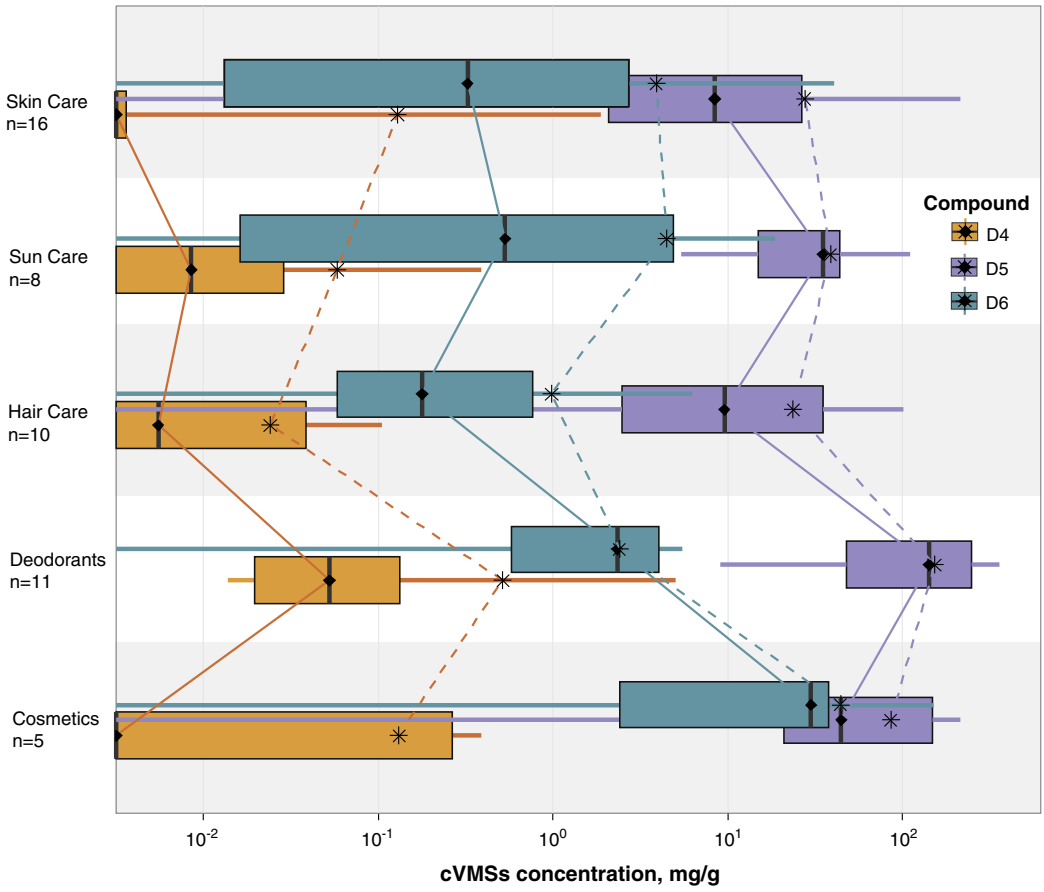

Fig. 1. Summary statistics of measured cVMS concentrations in cosmetics and personal care products sold in Europe by product category. The boxes in the plot represent the interquartile range. The right and left edges of the box indicate the 75th and 25th percentile of the data set, respectively. The ends of the horizontal lines indicate the maximum and minimum values observed. Solid and dashed colored lines link the medians and means of cVMS concentrations found in different product categories, respectively. Among all three compounds D5 has the highest mean and median concentrations.

cVMSs can be labeled on the ingredient list either as pure substances or nonspecifically as cyclomethicone. In order to investigate, if the label cyclomethicone can be associated with a specific mixture of cVMSs, we examined how the concentrations of different cVMSs are related to each other and to the labeling. Therefore, the products with detectable amounts of cVMSs were subdivided into three different groups (Table 2). A moderately positive correlation was found between the mean concentrations of D4 and D5 for the whole data set ($n = 48$; Pearson's correlation coefficient $r = 0.61$, $p < 0.01$). A slightly higher Pearson's correlation coefficient was observed between mean D4 and D5 if only the cyclomethicone-labeled products are considered ($n = 13$; $r = 0.70$, $p < 0.01$). In addition, it was found that D6 associates with cyclomethicone slightly stronger than D4, although the difference was not significant (100% cases vs. 76% for D6 and D4, respectively).

Table 2
Pearson correlation coefficients among concentrations of cVMSs measured in cosmetics and personal care products.

	Product group	Compound	D4	D5
1	All products that contained detectable amounts of cVMSs ($n = 48$)	D5	0.61*	
		D6	−0.02	−0.03
2	Products labeled with cyclomethicone only ($n = 13$)	D5	0.70*	
		D6	0.03	0.05
3	Products labeled with D5 only ($n = 27$)	D5	0.54*	
		D6	0.45*	0.89*

* Significant correlation ($p < 0.01$).

Furthermore, the variation in cVMS concentration ratios was different for the following two data subsets: 1) the subset that included the cyclomethicone labeled products only ($n = 13$), and 2) the subset that comprised the products labeled solely with D5, excluding the aforementioned liquid make-up outlier sample ($n = 27$). In the first data subset the spread in D5/D6 concentration ratios over different product subcategories was large and reached two orders of magnitude with the largest variation in the face cream subcategory (coefficient of variation $CV = 1.22$). In the second subset both concentration ratios fluctuated around 100 or 1000, which is in accordance with the definition of D5 that allows for <1% impurities of D6 and D4. These impurities are likely to be the by-products that originate from the industrial production of cVMSs (CES, 2010; O'Lenick, 2008).

3.2. Worst case assessment of aggregate dermal consumer exposure to D4 and D5

Different approaches exist to calculate consumer dermal exposure. The methods range from employing very simple deterministic exposure models to utilizing more sophisticated probabilistic frameworks. In the present work, daily exposure to D4 and D5 through application of eight most commonly used C&PCP subcategories (i.e. body lotion, face cream, hand cream, non-spray deodorant/antiperspirant, liquid foundation, rinse-off hair conditioner, sunscreen cream and sunscreen spray) was estimated (Table 3) using the Ford dermal exposure model (Ford, 1998). The exposure was calculated using both median and max D4/D5 concentrations in the product subcategories analyzed in

Table 3
Calculations of external daily dermal exposure (mg/capita/day) to cVMSs contained in selected cosmetics and personal care products.

Product [a]	Daily usage, g/capita/day (Ref.)		Freq. of use, 1/day[d]	Skin surface area exposed[e]		Ret. factor[f]	cVMS concentration, mg/g			Daily external exposure, mg/capita/day	
				cm^2	Description			D4	D5	D4	D5
Deo/antiperspirant non-spray	0.82[b]	Hall et al. (2007)	2	200	Both axillae	1	Median	0.066	187	0.05	153
	1.51[c]						Max	5.0	356	7.6	538
Face cream	0.85	Hall et al. (2007)	2.14	565	1/2 area head (female)	1	Median	0.00071[g]	24.7	0.001	21.0
	1.54						Max	1.9	214	2.9	330
Body lotion	4.56	Hall et al. (2007)	2.28	15,670	Area whole body without area head (female)	1	Median	0.00071[g]	15.0	0.003	68.4
	7.82						Max	0.015	28.3	0.12	221
Liquid foundation	0.17	Hall et al. (2011)	1	565	1/2 area head (female)	1	Median	0.13	96.5	0.02	16.4
	0.51						Max	0.39	213	0.20	109
Hand cream	0.87	Hall et al. (2011)	2	860	Area hands	1	Median	0.00071[g]	1.4	0.0006	1.22
	2.16						Max	0.00071[g]	12.5	0.002	27.0
Hair conditioner rinse-off	1.56	SCCS (2012)	0.28	1440	Area hands plus 1/2 area head	0.01	Median	0.00071[g]	6.4	0.00001	0.10
	3.92						Max	0.013	10.3	0.0005	0.40
Sunscreen cream	18.0	SCCNFP (2000)	2	17,500	Area whole body	1	Median	0.00071[g]	25.3	0.013	455
	18.0						Max	0.00071[g]	62.8	0.013	1130
Sunscreen spray	18.0	SCCNFP (2000)	2	17,500	Area whole body	1	Median	0.033	37.4	0.59	673
	18.0						Max	0.39	110	7.0	1980
Aggregate exposure: (excluding sunscreen products)							Median			0.08	260
							Max			10.8	1224

[a] Assuming 100% of the products in a category contain D4/D5.
[b] The 50th percentile of the daily product amount.
[c] The 90th percentile of the daily product amount (conservative approach).
[d] SCCS, 2012.
[e] From Bremmer et al. (2005).
[f] Retention factor is introduced to account for dilution and wash-off of the product with water (SCCS, 2010).
[g] Concentration is <LOQ; corresponding LOQ value is taken.

this study multiplied by the 50th or 90th percentiles, respectively, of the daily applied amounts of the products determined for the European population (Hall et al., 2007, 2011; SCCNFP, 2000; SCCS, 2012) and corrected by the retention factor to account for product dilution in water and/or wash-off where applicable.

The worst-case daily dermal (chronic) exposure for D4 and D5 from the use of personal care products investigated in this study was 10.8 and 1224 mg/capita/day, respectively. The sunscreens were not considered in this aggregate daily average dermal exposure assessment because they are usually applied on a short time scale (e.g. summer holidays), thus are most relevant for acute exposure. Assuming 0.5% and 0.04% dermal absorption rates for D4 and D5 (Jovanovic et al., 2008), the maximum dermal doses available for systemic absorption would be 0.054 and 0.49 mg/capita/day, respectively. Among considered product subcategories the main contributor to total maximum dermal exposure of cVMSs was a non-spray deodorant/antiperspirant (7.6 and 538 mg/day accounting for 70% and 44% of the aggregate daily dermal exposure to D4 and D5, respectively). Relatively high dermal exposure to both cVMSs occurs from the use of face creams, body lotions and liquid foundations with 27% (both D4 and D5), 1.0% (D4) and 18% (D5), 2.0% (D4) and 9.0% (D5) of the total dermal dose, respectively. Hand creams and rinse-off conditioners add less than 2.2% to the total daily dermal exposure to D5. Exposure to D4 from these product subcategories is also negligible and does not exceed a few hundred micrograms per day.

Overall, the results of the preliminary aggregate consumer exposure assessment indicate that the median dermal exposure to cVMSs is approximately 100 times lower than the NOAEL derived from chronic inhalation rat studies (i.e. 343 and 430 mg/kg/day for D4 and D5, respectively (Siddiqui et al., 2007a,b)).

4. Discussion

4.1. Comparison of the European data on cVMSs in C&PCPs with those from other studies

The emphasis of our study was given to the analysis of only selected product categories of specific brands that at present are most frequently used by consumers. In Fig. 2 we compare the results of the present study with those from previous publications, in which cVMS concentrations in C&PCPs, purchased in different countries, were investigated. Overall, our findings are in agreement with the results of Horii and Kannan (2008) and Wang et al. (2009), who report that D5 and D6 are the two predominantly used cyclic siloxanes in cosmetics and personal care products; D4 was found in smaller amounts and presumably in most cases as an impurity of D5 or D6. On the other hand, the maximum cVMS concentrations that we determined for skin care, hair care, deodorants and cosmetics were generally higher compared to those found in previous experimental studies (Horii and Kannan, 2008; Lu et al., 2011; Wang et al., 2009). For example, our maximum D5 concentrations in all product categories are approximately five times higher than those reported by Horii and Kannan (2008). The same tendency is observed when we compare our values with the results published by Wang et al. (2009), who analyzed 252 C&PCPs bought in Canada. Only for hair care products the concentrations differ by one and two orders of magnitude for D5 and D6, respectively. This is likely due to the fact that Wang et al. (2009) did not consider leave-on products (e.g., hair repair sprays) that usually employ cVMSs as their main constituents/carrier fluids (http://www.cosmetic-ingredients.net). Fig. 2 suggests that the U.S. and Canadian markets of C&PCPs are remarkably

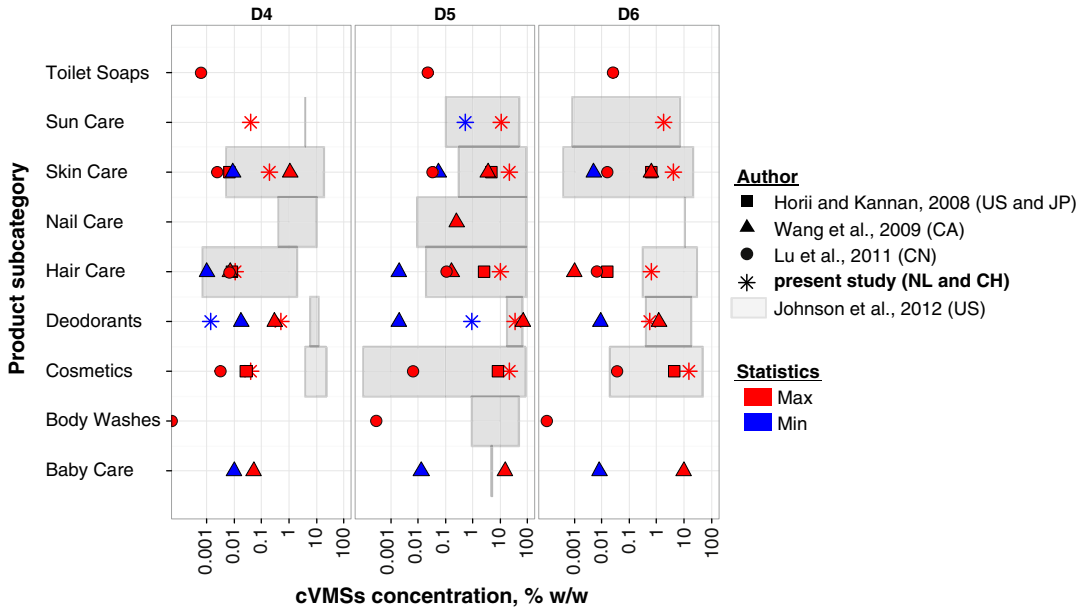

Fig. 2. The concentrations of cVMSs (minimum — blue and maximum — red) measured in different studies (Horii and Kannan, 2008 (USA and Japan); Wang et al., 2009 (Canada); Lu et al., 2011 (China) and present study (the Netherlands and Switzerland)) by product categories. For the studies in which the lowest values were below LOQ the minimum statistics are not shown. Semi-transparent bars represent the cVMS concentration ranges specified in the Cosmetic Ingredient Review report (Johnson et al., 2012).

similar in terms of cVMS levels. Besides, it shows that the personal care products sold in Europe contain comparable amounts of cVMSs; however, it is acknowledged that within the last five years cVMS concentrations in C&PCPs may have slightly increased, and therefore the concentrations found in the present study were higher. Interestingly, similar to the findings of Horii and Kannan (2008) we observe strong correlations among the concentrations of all three cVMSs for those products that were labeled with D5.

The study by Lu et al. (2011) surveying the Chinese market of C&PCPs (n = 158) showed considerably lower maximum measured concentrations of all three cVMSs in C&PCPs, for which two possible explanations may exist. First, the products in China may not contain high amounts of cVMSs because they are substituted with long-chain linear siloxanes, e.g., dimethicone, which is supported by Lu et al. (2010), who discovered that linear siloxanes dominate in the indoor dust in China. Second, our method of cVMS extraction from C&PCPs was slightly different, i.e. in their study Lu et al. used *n*-hexane only, which might have led to lower extraction efficiencies of the cVMSs from skin care products and cosmetics. However, given the limited sample size in our study, any apparent differences in maximum cVMS concentrations have to be interpreted with caution.

Our maximum measured D5 and D6 concentrations agree well with the concentration ranges declared by C&PCP manufacturers in the CIR report (Johnson et al., 2012), though it should be noted that our measured maximum D5 concentrations are close to the upper limits of this report. Conversely, D4 appears to be used in much higher amounts than our findings suggest (see Fig. 2), especially in deodorants (10-fold difference in D4 concentrations), cosmetics and sun care products (two orders of magnitude difference in D4 concentrations for both product categories). D4 is the most volatile congener (vapor pressure of 132 Pa at 25 °C) among the cVMSs analyzed, so that the discrepancy may partially be invoked by D4 volatilization losses during sample treatment (the volatility of the internal standard M4Q with vapor pressure of 9.0 Pa at 25 °C rather matches the vapor pressures of D5 and D6 with 33.2 and 4.6 Pa at 25 °C, respectively). However, the observed 10 and 100-fold difference in D4 concentrations cannot be explained by evaporation, because the recovery rates of D4 from the reference products were larger than 80% (see Fig. SI-1 of the Supplementary Information).

The deviations in D5/D4 and D5/D6 concentration ratios in different C&PCPs suggest that cosmetics formulators do not abide particular proportions of individual cVMSs in the cyclomethicone ingredient, but rather that it stands for variable mixtures of low molecular weight volatile cyclic siloxanes (also confirmed by Verbiese, 2012).

Finally, the comparison of five selected products purchased in two different European countries suggests that cVMS levels may not always be the same even in products of the same brand name that seem identical at first glance. Hence, the concentrations of cVMSs determined in our study should be generalized with caution due to both spatial and temporal variation in the availability of marketed products and brands within the European Union.

Overall, the calculated external dermal exposure to cVMSs is in line with the findings of Buser et al. (2013), who measured cVMS concentrations in ambient air in Zurich, Switzerland and back-calculated the average emission rates of D5 and D6 (which originate exclusively from use of C&PCPs). Their results were 310 and 36 mg/capita/day for D5 and D6, respectively when adjusted for the population of Zurich (i.e. ~400,000 citizens). Furthermore, our dermal exposure estimates are comparable to those reported for the U.S., Japan, and Canada: absolute values of aggregate external dermal exposure to D4 and D5 for women in the U.S. (Horii and Kannan, 2008) were 1.1 and 233 mg/day, respectively, 98.6 and 900 mg/day in Canada (Wang et al., 2009), whereas in China women are exposed to only 4.5 mg/day of total (i.e. four cyclic and 11 linear) siloxanes from the use of personal care products (Lu et al., 2011).

4.2. Additional implications for consumer exposure assessment

This product survey of 51 consumer products was designed to generate data that can be used in a consumer exposure assessment. In contrast to the common practice of choosing the products for a product survey at random (FAO/WHO, 2004) we based our choice on a screening assessment of consumer exposure (see SI, Table SI-2). By this procedure we were able to focus our experimental efforts on the products that contribute most to adult consumer exposure. In particular, we included sun care products, which had never been analyzed for cVMSs in the past, but were shown to contribute substantially to acute consumer exposure (see SI, Table SI-3). Similarly, we did not analyze

bath/shower and nail care products, because their contribution to cVMS consumer exposure is negligible. Also, we did not include childcare products, since our focus is on adult exposure. However, it should be kept in mind that apart from the targeted product categories other C&PCPs that had not been investigated in this study (e.g., perfumes, shampoos, and hairstyling products) may contain trace amounts of cVMSs as impurities of linear siloxanes, although their contribution to aggregate daily consumer exposure is expected to be insignificant.

Our study aimed at deriving the most typical values for the cVMS content in different product subcategories, thus further specifying the concentration ranges that are given as frame formulations (CPNP, 2013). Therefore, we intentionally selected the products with cVMSs labeled on their ingredient list, so that the exposure estimates are not biased by zero values determined for the compound-free products. Declaredly, the assumption of 100% occurrence of cVMSs in all C&PCPs may result in the overestimation of aggregate consumer exposure. However, the aim of this study was to obtain "typical" cVMS concentrations that are independent of the alternating fraction of cVMS-containing products on the market. We used the concentrations to calculate a standard worst case exposure. Since the comparison with current NOAEL shows a safety factor of 100 for both D4 and D5, no further refinements, like e.g. including the market fractions of cVMS-containing products, are necessary.

If a more realistic aggregate exposure assessment is needed the "typical" concentrations determined for each product (sub)category can be corrected for their respective market fraction. The market fractions can be sourced from numerous marketing studies and databases, e.g. Global New Products Database (Mintel Group Ltd). Also, Horii and Kannan (2008) and Lu et al (2011) investigated the frequency of occurrence of cosmetics and personal care products that contain cVMSs. They found that 50–87% of the randomly selected C&PCPs contain D4, 57–91% contain D5 and 50–90% contain D6. The detection frequencies of cVMSs also depend on the category and were 90%, 35% and 25% for antiperspirants, skin lotions and hair care products, respectively (Wang et al., 2009).

5. Conclusions

Cosmetics and personal care products (C&PCPs) analyzed in this study contained varying concentrations of D4, D5, and D6. Among these three cVMSs the concentrations of D5 were the highest in all product categories and ranged between 0.01% w/w in hand creams and more than 35% w/w in deodorants. Concentrations of D4 were much lower, suggesting that it is mostly present as an impurity of higher order cVMSs. Sparse presence of D4 in C&PCPs found in this study also supports the industry statements of phasing out D4 and replacing it with the less toxic D5 and D6. However, the comparison between the results of the present study and the others shows that the use of cVMSs, and D5 in particular, in C&PCPs is continuously rising. Overall, deodorants/antiperspirants and liquid foundations had the highest mean and median concentrations of all three cVMSs. Deodorants/antiperspirants were also shown to contribute the most to aggregate daily dermal cVMS exposure. The high concentrations of cVMSs in C&PCPs found in the present study identify the use of cosmetics and personal care products as the primary source of cVMS exposure for humans and the environment.

Acknowledgments

Yanhua Chen is gratefully acknowledged for helping with the initial method development, and Andreas Dutly from ETH Zürich for providing technical assistance. We would also like to thank Unilever for disclosing the information about the cVMS concentrations in the reference products.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.envint.2013.10.002.

References

Biesterbos JWH, Dudzina T, Delmaar CJE, Bakker M, Russel FGM, von Goetz N, et al. Usage patterns of personal care products: important factors for exposure assessment. Food Chem Toxicol 2013;55:8–17.

Bremmer HJ, Prud'Homme de Lodder LCH, van Engelen JGM. Cosmetics fact sheet to assess the risks for the consumer, updated version for ConsExpo4. RIVM Report 320104 001/2005; 2005.

Burns-Naas LA, Mast RW, Meeks RG, Mann PC, Thevenaz P. Inhalation toxicology of decamethylcyclopentasiloxane (D5) following a 3-month nose-only exposure in Fischer 344 rats. Toxicol Sci 1998;43(2):230–40.

Burns-Naas LA, Meeks RG, Kolesar GB, Mast RW, Elwell MR, Hardisty JF, et al. Inhalation toxicology of octamethylcylotetrasiloxane (D4) following a 3-month nose-only exposure in Fisher 344 rats. Int J Toxicol 2002;21:39–53.

Buser AM, Kierkegaard A, Bogdal C, MacLeod M, Scheringer M, Hungerbühler K. Concentrations in ambient air and emissions of cyclic volatile methylsiloxanes in Zurich, Switzerland. Environ Sci Technol 2013. http://dx.doi.org/10.1021/es3046586. [in print].

Centre Européen des Silicones (CES). Cyclic Polymerization. Available online at http://www.silicones-science.com/chemistry/polydimethylsiloxanes-pdms/cyclic-polymerisation, 2010. [last accessed on 01.02.2013].

Centre Européen des Silicones (CES). The Industry: Facts and Figures. Available online athttp://www.silicones.eu/the-industry/facts-figures, 2011. [last accessed on 01.02.2013].

Cosmetic Products Notification Portal (CPNP). Article 13 User Manual. Annex II: Frame formulations. Available online athttp://ec.europa.eu/consumers/sectors/cosmetics/files/pdf/cpnp_user_manual_en.pdf, 2013. [last accessed on 01.07.2013].

Dow Corning Corporation. Summary of toxicology on cyclic and linear diemthylsiloxane oligomers and polymers; 1986 [March 14, 1986 [cited in ICLID 2000, ref. 53]].

Dow Corning Corporation. 24-month combined chronic toxicity and oncogenicity whole body vapor inhalation study of octamethylcyclotetrasiloxane (D4) in Fischer 344 rats. Report No. 2004-10000-54091; 2004.

Dow Corning Corporation. Decamethylcyclopentasiloxane (D5): a 24-month combined chronic toxicity and carcinogenicity whole body vapor inhalation study in Fischer 344 rats. Study No. 9346, Report No. 2003-10000-53252; 2005.

Environmental Working Group (EWG). Available online at http://www.ewg.org/skindeep/ingredient/products/, 2012. [last accessed on 01.02.2013].

European Chemical Agency (ECHA). Identification of PBT and vPvB substance. Results of evaluation of PBT/vPvB properties for decamethylcyclopentasiloxane; 2012 [Available online at http://echa.europa.eu/documents/10162/13628/decamethyl_pbtsheet_en.pdf (last accessed 01.06.2013)].

European Food Safety Authority (EFSA). Management of left-censored data in dietary exposure assessment of chemical substances. EFSA J 2010;8(3):1557.

Falany CN, Li G. Effects of age and pregnancy on cytochrome P450 induction by octamethyltetracyclosiloxane in female Sprague–Dawley rats. J Biochem Mol Toxicol 2005;19(2):129–38.

FAO/WHO (Food and Agriculture Organization of the United Nations). The Codex general guidelines on sampling — CAC/GL 50-2004; 2004.

Flassbeck D, Pfleiderer B, Grumping R, Hirner AV. Determination of low molecular weight silicones in plasma and blood of women after exposure to silicone breast implants by GC/MS. Anal Chem 2001;73:606–11.

Ford RA. The human safety of the polycyclic musks AHTN and HHCB in fragrances — a review. Dtsch Lebensmitt Rundsch 1998;94(8):268–75.

Genualdi S, Harner T, Cheng Y, MacLeod M, Hansen KM, van Egmond R, et al. Global distribution of linear and cyclic volatile methyl siloxanes in air. Environ Sci Tech 2011;45:3349–54.

Goddard DE, Gruber JV. Principles of polymer science and technology in cosmetics and personal care. Cosmetic Science and Technology Series, Volume 22. Marcel Dekker, Inc.; 1999 [Available online at http://rgmaisyah.files.wordpress.com/2009/02/principles-of-polymer-science-and-technology-in-cosmetics-and-personal-care.pdf (last accessed 01.08.2013)].

Gouin T, van Egmond R, Sparham C, Hastie C, Chowdhury N. Simulated use and wash-off release of decamethylcyclopentasiloxane used in antiperspirants. Chemospher 2013;93(5):726–34.

Hall B, Tozer S, Safford B, Coroama M, Steiling W, Leneveu-Duchemin MC, et al. European consumer exposure to cosmetic products, a framework for conducting population exposure assessments. Food Chem Toxicol 2007;45:2097–108.

Hall B, Steiling W, Safford B, Coroama M, Tozer S, Firmani C, et al. European consumer exposure to cosmetic products, a framework for conducting population exposure assessments Part 2. Food Chem Toxicol 2011;49:408–22.

Hanssen L, Warmer NA, Braathen T, Odland JO, Lund E, Nieboer E, et al. Plasma concentrations of cyclic volatile methylsiloxanes (cVMS) in pregnant and postmenopausal Norwegian women and self-reported use of personal care products (PCPs). Environ Int 2013;51:82–7.

Health Canada. Screening assessment for the challenge. Decamethylcyclopentasiloxane (D5), CAS 541-02-6. Environment Canada, Health Canada; 2008 [Available online at http://www.ec.gc.ca/substances/ese/eng/challenge/batch2/batch2_541-02-6.cfm (last accessed on 01.02.2013)].

Horii Y, Kannan K. Survey of organosilicone compounds, including cyclic and linear siloxanes, in personal care and household products. Arch Environ Contam Toxicol 2008;55:701–10.
Jäger R, Hartmann E. Subchronische toxikologische Untersuchungen an Ratten (Magensondenapplikation über 13 Wochen). In: Bayer AG, editor. Report no. 20204; 1991. [May 3, 1991].
Johnson W, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Liebler DC, et al. Safety assessment of cyclomethicone, cyclotetrasiloxane, cyclopentasiloxane, cyclohexasiloxane, and cycloheptasiloxane. Int J Toxicol 2012;30(6 Suppl.): 149S–227S.
Jovanovic ML, McMahon JM, McNett DA, Tobin JM, Plotzke KP. In vitro and in vivo percutaneous absorption of 14C-octamethylcyclotetrasiloxane (14C-D4) and 14C-decamethylcyclopentasiloxane (14C-D5). Regul Toxicol Pharmacol 2008; 50:239–48.
Kaj L, Schlabach M, Andersson J, Cousins AP, Schmidbauer N, Brorström-Lundén E. Siloxanes in the Nordic environment. Norden; 2005a [Available online at http://www.norden.org/da/publikationer/publikationer/2005-593/at_download/publicationfile (last accessed on 01.02.2013)].
Kaj L, Andersson J, Cousins AP, Remberger M, Brorström-Lundén E. Results from the Swedish National Screening Programme 2004. Subreport 4: siloxanes. Swedish Environmental Research Institute (IVL); 2005b. [Available online at http://www.imm.ki.se/Datavard/PDF/B1643_siloxaner.pdf (last accessed on 01.02.2013)].
Kala SV, Lykissa ED, Lebovitz RM. Detection and characterization of poly(dimethylsiloxanes) in biological tissues by GC/AED and GC/MS. Anal Chem 1997;69:1267–72.
Lu Y, Yuan T, Yun SH, Wang W, Wu Q, Kannan K. Occurrence of cyclic and linear siloxanes in indoor dust from China, and implications for human exposures. Environ. Sci. Technol. 2010;44:6081–7.
Lu Y, Yuan T, Wang W, Kannan K. Concentrations and assessment of exposure to siloxanes and synthetic musks in personal care products from China. Environ Pollut 2011;159(12):3522–8. [Epub 2011 Sep 3526].
Maddalena R, McKone T, Destaillats H, Rusell M, Hodgson A, Perino C. Quantifying pollutant emissions from office equipment: a concern in energy-efficient buildings. California Energy Commission, PIER Energy-Related Environmental Research; 2011 [CEC-500-2011-046. [Available online at http://www.energy.ca.gov/2011publications/CEC-500-2011-046/CEC-500-2011-046.pdf (last accessed on 01.02.2013)]].
McLachlan MS, Kierkegaard A, Hansen KM, van Egmond R, Christensen JH, Skioth CA. Concentrations and fate of decamethylcyclopentasiloxane (D5) in the atmosphere. Environ. Sci. Techol. 2010;44:5365–70.
Mintel Group Ltd. Global New Products Database. Available online athttp://www.gnpd.com. [(last accessed 01.05.2013) on a commercial basis].
NILU. Siloxanes in the environment of the Inner Oslofjord. Norsk Institutt for Luftforsking; 2007 [Available online at http://www.sft.no/publikasjoner/2269/ta2269.pdf (last accessed on 01.02.2013)].
Norden. Siloxanes in the Nordic environment. Copenhagen: Nordic Council of Ministers; 2005 [TemaNord 2005:593. [Available online at http://www.norden.org/pub/miljo/miljo/uk/TN2005593.pdf (last accessed on 01.02.2013)]].
OECD. The 2007 OECD List of High Production Volume Chemicals. Available online at http://search.oecd.org/officialdocuments/displaydocumentpdf/?cote=ENV/JM/MONO(2009)40&doclanguage=en, 2007. [last accessed on 01.02.2013].
O'Lenick AJ. Silicones for personal care; 2008.
Reddy MB, Andersen ME, Morrow PE, Dobrev ID, Varaprath S, Plotzke KP, et al. Physiological modeling of inhalation kinetics of octamethylcyclotetrasiloxane in humans during rest and exercise. Toxicol Sci 2003;72:3–18.
Reddy MB, Looney RJ, Utell MJ, Plotzke KP, Andersen ME. Modeling of human dermal absorption of octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5). Toxicol Sci 2007;99:422–31.
Reddy MB, Dobrev ID, McNett DA, Tobin JM, Utell MJ, Morrow PE, et al. Inhalation dosimetry modeling with decamethylcyclopentasiloxane in rats and humans. Toxicol Sci 2008;105:275–85.
SCCNFP (Scientific Committee on Cosmetic Products, Non-Food products intended for Consumers). Notes of guidance for testing of cosmetic ingredients for their safety evaluation, 4th revision. SCCNFP/0321/00. Adopted by the SCCNFP during the plenary meeting of 24 October 2000; 2000.
SCCS (Scientific Committee on Consumer Safety). Opinion on cyclomethicone, octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5). Available online athttp://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_029.pdf, 2010. [last accessed on 01.02.2013].
SCCS (Scientific Committee on Consumer Safety). The SCCS's notes of guidance for the testing of cosmetic ingredients and their safety evaluation. 8th revision. SCCS/1501/12. Available online athttp://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_006.pdf, 2012. [last accessed on 01.02.2013].
Siddiqui WH, Stump DG, Plotzke KP, Holson JF, Meeks RG. A two-generation reproductive toxicity study of octamethylcyclotetrasiloxane (D4) in rats exposed by whole body vapor inhalation. Reprod Toxicol 2007a;23(2):202–15.
Siddiqui WH, Stump DG, Plotzke KP, Holson JF, Meeks RG. A two-generation reproductive toxicity study of decamethylcyclopentasiloxane (D5) in rats exposed by whole body vapor inhalation. Reprod Toxicol 2007b;23(2):216–25.
Sparham C, Van Egmond R, O'Connor S, Hastie C, Whelan M, Kanda R. Determination of decamethylcyclopentasiloxane in river water and final effluent by headspace gas chromatography/mass spectrometry. J Chromatogr A 2008;1212:124–9.
Tuomainen A, Seuri M, Sieppi A. Indoor air quality and health problems associated with damp floor coverings proceedings. Indoor Air 2002;137:41.
U.S. Environmental Protection Agency (U.S. EPA). Non-confidential inventory update reporting production volume information. Toxic Substances Control Act (TSCA) Inventory; 2002 [Available online at http://www.epa.gov/oppt/iur/tools/data/2002-vol.htm (last accessed on 01.02.2013)].
U.S. Environmental Protection Agency (US EPA). Broad scan analysis of the FY82 National Human Adipose Tissue Survey Specimens. EPA-560/5-86-035, December 1986; Characterization of HRGC/MS Unidentified Peaks from the Analysis of Human Adipose Tissue; 1987 [EPA-560/5-87-002A, May].
UK Environmental Agency (UK EA). Environmental risk assessment report on octamethylcyclotetrasiloxane. Available online at http://cdn.environment-agency.gov.uk/scho0309bpqz-e-e.pdf, 2009. [last accessed on 01.02.2013].
UK Environmental Agency (UK EA). Environmental risk assessment report on decamethylcyclopentasiloxane. Available online at http://cdn.environment-agency.gov.uk/scho0309bpqx-e-e.pdf, 2009. [last accessed on 01.02.2013].
UK Environmental Agency (UK EA). Environmental risk assessment report on dodecamethylcyclohexasiloxane. Available online at http://cdn.environment-agency.gov.uk/scho0309bpqy-e-e.pdf, 2009. [last accessed on 01.02.2013].
Verbiese N. Dow Corning Corporation. Personal communication; 2012.
Wang R, Moody RP, Koniecki D, Zhu L. Low molecular weight cyclic volatile methylsiloxanes in cosmetic products sold in Canada: implication for dermal exposure. Environ Int 2009;35(6):900–4. [Epub 2009 Apr 2010].
Warner NA, Evenset A, Christensen G, Gabrielsen GW, Borga K, Leknes H. Volatile siloxanes in the European Arctic: assessment of sources and spatial distribution. Environ. Sci. Technol. 2010;44:7705–10.
Yucuis RA, Stanier CO, Hornbuckle KC. Cyclic siloxanes in air, including identification of high levels in Chicago and distinct diurnal variation. Chemosphere 2013;92(8):905–10.
Zhang Z, Qi H, Ren N, Li Y, Gao D, Kannan K. Survey of cyclic and linear siloxanes in sediment from the Songhua River and in sewage sludge from wastewater treatment plants, Northeastern China. Arch Environ Contam Toxicol 2011;60:204–11.