Supporting Information

The probabilistic aggregate consumer exposure model (PACEM): validation and comparison to a lower-tier assessment for the cyclic siloxane D5

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1. Lower tier screening exposure assessment

The lower tier implements general principles for conservative consumer exposure assessment (European Chemicals Agency (ECHA), 2012; Scientific committee on consumer safety (SCCS), 2012) including frequent and extensive product use on a regular basis under unfavorable circumstances (e.g. application and subsequent long stay in a small unventilated room). The release and subsequent fate of D5 are governed by the following worst-case assumptions: 1) the release is instantaneous; and 2) there is no removal of the substance. Exposure calculations were executed for a standard (adult) person with the body weight of 60 kg, whole body surface area of 17,500 cm^2 and inhalation rate of 26 m^3/day (Bremmer, 2006a). The equations used for the calculations of reasonable worst-case consumer exposure via different routes are provided below.

Inhalation:

$$C_{inh} = \frac{Q_{prod} \cdot Fc_{prod}}{V_{room}}$$

$$D_{inh} = \frac{F_{resp} \cdot C_{inh} \cdot IH \cdot T_{contact} \cdot FQ}{BW}$$

Input Parameter	Description	Unit	Default
Q_{prod}	Amount of product used	[mg]	
Fc_{prod}	Weight fraction of D5 in a product	[g/g_{prod}]	
V_{room}	Room volume	[m^3]	2
F_{resp}	Respirable fraction of inhaled D5	[-]	1
IH	Inhalation rate of a person	[m^3/day]	26
$T_{contact}$	Duration of contact per event	[day]	
FQ	Frequency of use	[1/day]	
BW	Body weight of a person	[kg]	60
Output Parameter	**Description**	**Unit**	
C_{inh}	Concentration of D5 in room air	[mg/m^3]	
D_{inh}	Inhalatory dose	[mg/kg bw/day]	

Dermal:

$$D_{der} = \frac{Q_{prod} \cdot Fc_{prod} \cdot A_{abs} \cdot FQ \cdot Rf}{BW}$$

Input Parameter	Description	Unit	Default
Q_{prod}	Amount of product used	[mg]	
Fc_{prod}	Weight fraction of D5 in a product	[g/g_{prod}]	
A_{abs}	Dermal absorption fraction	[-]	1
FQ	Frequency of use	[1/day]	
Rf	Retention factor	[-]	
BW	Body weight of a person	[kg]	60
Output Parameter	**Description**	**Unit**	
D_{der}	Dermal dose	[mg/kg bw/day]	

Oral:

$$D_{oral} = \frac{V \cdot D \cdot Fc_{prod} \cdot FQ}{BW}$$

Input Parameter	Description	Unit	Default
V	Volume of product swallowed	[cm^3]	
D	Density of product	[mg/cm^3]	1
Fc_{prod}	Weight fraction of D5 in a product	[-]	
FQ	Frequency of use	[1/day]	
BW	Body weight of a person	[kg]	60
Output Parameter	**Description**	**Unit**	
D_{oral}	Oral dose	[mg/kg bw/day]	

Only cosmetics and personal care products (C&PCPs) were considered in the lower tier assessment; other products (e.g. sealants, dry-cleaned textiles) are expected to contribute only marginally to aggregate consumer exposure. C&PCPs were allocated into 51 categories characterized with unique application scenarios. Both acute (on the day of use) and chronic (yearly average) aggregate external exposures were calculated route-wise. Complementary to dermal, oral and direct inhalation exposure, indirect inhalation of D5 vapour, occurring when the substance evaporates from consumers' skin after product application (referred hereafter as 'evaporation scenario') was modelled. Following the Canadian risk assessment for D5 (Environment and Health Canada, 2008) it was assumed that 20% of the dermally applied amount evaporates instantaneously and becomes available for inhalation. The external exposures via different routes were multiplied by the route-specific absorption fractions (Table SI-1). Aggregation of exposure was performed over all considered C&PCP categories. However, to avoid unreasonable overestimation of exposure, amongst product categories with similar application purpose (e.g. deodorant spray and deodorant stick) the one with the highest exposure value was selected. This yielded 43 maximum possible C&PCPs categories that can potentially be used by a consumer on a daily basis. The higher tier model is based on data that include the co-use of products. Therefore, in PACEM we did not need to reduce the number of categories by the ones used interchangeably. Still, we reduced the number of 51 categories to 47 on the basis of an analytical study that revealed that in some product categories D5 is not used.

The main sources for the input data were Cosmetics Europe studies (Hall et al., 2011; Hall et al., 2007; McNamara et al., 2007), SCCS's notes of guidance for testing of cosmetic ingredients and their safety

evaluation, and RIVM Cosmetics Fact Sheet (Bremmer, 2006b) listed in the order of their priority. Reasonably conservative values (P75s) were chosen for the product use amounts and use frequencies. D5 concentrations in each C&PCP category were obtained from cosmetic frame formulations (European Commission (EC), 2013), which list the ingredients' group and typical (maximum) concentration in 'generic' cosmetic products. We assumed that all C&PCPs used by a standard consumer would contain D5. The default input values for each C&PCP category considered are listed in Table SI-2.

Both acute (on the day of use) and chronic (yearly average) aggregate consumer exposure were calculated in the worst-case assessment for each route separately (Table SI-1). The internal exposure was determined using the highest reported route-specific uptake fractions identified from the literature. As Table SI-1 suggests, in spite of a 10-fold higher uptake fraction, inhalation contributes to the total chronic internal exposure only half of the dermal dose. Inclusion of the evaporation scenario (i.e. enhancement of the proportion of inhalation exposure) only slightly alters the final results: the total chronic systemic dose is reduced by less than 3%. The key contributors to aggregate chronic exposure to D5 are hair care, sun care products and deodorants via inhalation; body care, skin care, sun care products and deodorants via dermal application; and toothpaste and lip balm via inadvertent ingestion. Detailed results of the lower tier exposure modelling can be found in Tables SI-3,4.

Table SI - 1. Lower tier estimates of aggregate consumer exposure to D5

	Acute exposure, mg/kg_bw/day				**Chronic exposure, mg/kg_bw/day**			
	Inh	**Derm**	**Oral**	**Total**	**Inh**	**Derm**	**Oral**	**Total**
External exposure when evaporation of D5 not included	38.4	614	4.1	**656.5**	10.8	307	4.1	**321.9**
External exposure when evaporation of D5 included	42.6	491	4.1	**537.7**	12.5	246	4.1	**262.6**
Absorption/uptake fraction (%)	2.0	0.17	100		2.0	0.17	100	
Internal exposure when evaporation of D5 not included	0.77	1.04	4.10	**5.91**	0.22	0.52	4.10	**4.84**
Internal exposure when evaporation of D5 included	0.85	0.84	4.10	**5.79**	0.25	0.42	4.10	**4.77**
LOEL				**100.0**				**100.0**
Minimal margin of exposure (MoE)				**16.9**				**20.7**

Table SI-2. Input parameters used in the lower tier aggregate consumer exposure assessment to D5 from application of C&PCPs

Product category	Product subcategory	Substance weight fraction [a]	Amount of product sprayed, g/event (used only for direct inhalation exposure)	Amount of product applied on skin g/event	Frequency of use, events/day	Frequency of use, events/year	Retention factor
Hair Care	Shampoo	0.15		4.184	2	260	0.01
	Conditioner (rinse-off)	0.20		3.136	1	104	0.01
	Conditioner (leave-on) [b]	0.99		3.136	1	104	0.1
	Hair mask	0.50		3.136	1	104	0.01
	Hair styling (wax, mousse, gel)	0.99		3.2	2	358	0.1
	Fixative spray	0.50	1.02	0.48	2	438	0.1
	Detangle spray	0.50	1.02	0.48	1	104	0.1
	Semi-permanent dye	0		24	1	13	0.01
	Permanent dye (oxidative)	0		80	1	10	0.01
	Hair bleach [b]	0		160	1	10	0.01
	Permanent wave	0		128	1	4	0.01
Bath and Shower	Body wash (gel, cream, scrub)	0.01		7.5	2	329	0.01
	Hand soap (liquid and solid)	0.01		3.2	5	1825	0.01
	Bath foam, oil, salt	0.1		20.0	1	104	0.01
Body Care	Body lotion (cream, oil, milk)	0.90		3.13	2	730	1
	Body pack (mud mask)	0		332.8	1	4	0.01
Sun Care	Bronzer, sun-tan	0.20		3.128	1	39	1
	Sun screen (cream, lotion)	0.4		14.4	2	75	1
	Sun screen (spray) [b]	0.4	3.2	14.4	2	75	1
Skin Care	Face cream (day, night)	0.90		0.616	2	730	1
	Face whitening cream	0.90		0.616	1	91	1

Product category	Product subcategory	Substance weight fraction [a]	Amount of product sprayed, g/event (used only for direct inhalation exposure)	Amount of product applied on skin g/event	Frequency of use, events/day	Frequency of use, events/year	Retention factor
Foot Care	Antiperspirant (gel, cream)	0.3		0.96	2	730	1
	Antifungal gel, cream	0.20		0.08	1	90	1
Deodorant	Spray [b]	0.20	0.46	2.07	2	730	1
	Stick and roll-on	0.50		0.60	2	365	1
Shaving	Gel, foam	0.1		1.6	1	365	0.01
	Balm, balsam	0.2		0.96	1	365	1
Make-up	Mascara	0.800		0.02	1	365	1
	Eye shadow (liquid and powder)	0.700		0.008	2	730	1
	Eye liner	0.500		0.004	1	365	1
	Liquid foundation	0.40		0.408	1	365	1
	Compact powder	0.45		0.19	4	1460	1
	Remover	0.5		2	2	730	0.01
	Lipstick, lip balm	0.65		0.008	4	1460	1
Nail Care	Polish enamel, top and base coat	0.010		0.042	1	156	1
	Polish remover	0.010		0.17	1	156	1
Baby Care	Diaper cream	0.2		1.04	6	2190	1
	Talc	0.0		0.64	6	2190	1
	Tissues	0.0		2.4	5	1825	1
Fragrance	Eau de toilette (spray) [b]	0.01	0.11	0.49	3	1095	1
	Eau de perfume (spray)	0.01	0.03	0.16	2	237	1
Miscellaneous	Depilatory Cream	0.03		4.4	1	17	0.01
	Massage Essential Oil	0.30		3.1	1	24	1
	Bath Essential Oil	0.3		0.64	1	52	0.01

[a] – The substance's weight fractions in a particular C&PCP category were taken from COLIPA frame formulations (EC, 2013) and assigned to the category as a whole regardless of the product brands prevalent in the category. If explicitly specified the respective maximum level (% w/w) of silicone ingredients or emollients was chosen. If according to the frame formulations a product category does not contain silicone material or emollients, a conservative value of 1% w/w was assigned to this product category.

[b] - this product subcategory was selected amongst similarly shaded ones to calculate aggregate daily exposure

Table SI - 3. Results of the lower tier aggregate consumer exposure assessment to D5 from application of C&PCPs (evaporation scenario not included)

Product category	Product subcategory	Acute exposure (i.e. on the day of use), mg/kg_bw/day						Chronic exposure, mg/kg_bw/day					
		Inhalation		Dermal		Oral		Inhalation		Dermal		Oral	
		external	internal	external	internal	external	internal	external	internal	external	internal	external	internal
Hair Care	Shampoo			2.6E-01	4.4E-04					9.3E-02	1.6E-04		
	Conditioner (rinse-off)			1.3E-01	2.2E-04					3.7E-02	6.3E-05		
	Conditioner (leave-on) [a]			6.5E+00	1.1E-02					1.8E+00	3.1E-03		
	Hair mask			3.3E-01	5.6E-04					9.3E-02	1.6E-04		
	Hair styling (wax, mousse, gel)			1.3E+01	2.2E-02					6.5E+00	1.1E-02		
	Fixative spray	9.2E+00	1.8E-01	1.0E+00	1.7E-03			5.5E+00	1.1E-01	6.0E-01	1.0E-03		
	Detangle spray	4.6E+00	9.2E-02	5.0E-01	8.5E-04			1.3E+00	2.6E-02	1.4E-01	2.4E-04		
	Semi-permanent dye			7.5E-01	1.3E-03					2.7E-02	4.5E-05		
	Permanent dye (oxidative)			2.5E+00	4.3E-03					6.8E-02	1.2E-04		
	Hair bleach [a]			3.3E+00	5.7E-03					9.1E-02	1.6E-04		
	Permanent wave			1.9E+00	3.2E-03					2.0E-02	3.5E-05		
Bath and Shower	Body wash (gel, cream, scrub)			3.1E-02	5.3E-05					1.4E-02	2.4E-05		
	Hand soap (liquid and solid)			3.3E-02	5.7E-05					3.3E-02	5.7E-05		
	Bath foam, oil, salt			2.1E-01	3.6E-04					6.0E-02	1.0E-04		
Body Care	Body lotion (cream, oil, milk)			1.2E+02	2.0E-01					1.2E+02	2.0E-01		
	Body pack (mud mask)			6.9E-01	1.2E-03					7.6E-03	1.3E-05		
Sun Care	Bronzer, sun-tan			1.3E+01	2.2E-02					1.4E+00	2.4E-03		
	Sun screen (cream, lotion)			2.4E+02	4.1E-01					2.5E+01	4.2E-02		
	Sun screen (spray) [a]	2.3E+01	4.6E-01	2.4E+02	4.1E-01			2.4E+00	4.7E-02	2.5E+01	4.2E-02		
Skin Care	Face cream (day, night)			2.3E+01	3.9E-02					2.3E+01	3.9E-02		

Product category	Product subcategory	Acute exposure (i.e. on the day of use), mg/kg_bw/day						Chronic exposure, mg/kg_bw/day					
		Inhalation		Dermal		Oral		Inhalation		Dermal		Oral	
		external	internal	external	internal	external	internal	external	internal	external	internal	external	internal
	Face whitening cream			1.2E+01	2.0E-02					2.9E+00	4.9E-03		
	Hand cream			3.2E+01	5.5E-02					3.2E+01	5.5E-02		
	Eye cream			2.0E+00	3.5E-03					2.0E+00	3.5E-03		
	Facial cleanser (peeling, scrub)			1.3E-03	2.3E-06					3.8E-04	6.5E-07		
	Facial cleanser (tissues)			1.7E-01	2.9E-04					4.8E-02	8.2E-05		
	Face pack (peel-off mask)			6.7E+01	1.1E-01					1.9E+01	3.2E-02		
Oral Care	Toothpaste					3.0E-02	3.0E-02					3.0E-02	3.0E-02
	Mouthwash					3.6E+00	3.6E+00					3.6E+00	3.6E+00
Foot Care	Antiperspirant (gel, cream)			1.2E+01	2.0E-02					1.2E+01	2.0E-02		
	Antifungal gel, cream			3.3E-01	5.6E-04					8.1E-02	1.4E-04		
Deodorant	Spray [a]	1.7E+00	3.3E-02	1.7E+01	2.9E-02			1.7E+00	3.3E-02	1.7E+01	2.9E-02		
	Stick and roll-on			1.3E+01	2.1E-02					6.3E+00	1.1E-02		
Shaving	Gel, foam			3.0E-02	5.1E-05					3.0E-02	5.1E-05		
	Balm, balsam			4.0E+00	6.8E-03					4.0E+00	6.8E-03		
Make-up	Mascara			3.3E-01	5.6E-04					3.3E-01	5.6E-04		
	Eye shadow (liquid and powder)			2.3E-01	3.9E-04					2.3E-01	3.9E-04		
	Eye liner			4.2E-02	7.1E-05					4.2E-02	7.1E-05		
	Liquid foundation			3.4E+00	5.8E-03					3.4E+00	5.8E-03		
	Compact powder			7.1E+00	1.2E-02					7.1E+00	1.2E-02		
	Remover			4.2E-01	7.1E-04					4.2E-01	7.1E-04		
	Lipstick, lip balm			4.3E-01	7.3E-04	4.3E-01	4.3E-01			4.3E-01	7.3E-04	4.3E-01	4.3E-01
Nail Care	Polish enamel, top and base coat			8.8E-03	1.5E-05					3.7E-03	6.4E-06		

Product category	Product subcategory	Acute exposure (i.e. on the day of use), mg/kg_bw/day						Chronic exposure, mg/kg_bw/day					
		Inhalation		Dermal		Oral		Inhalation		Dermal		Oral	
		external	internal	external	internal	external	internal	external	internal	external	internal	external	internal
	Polish remover			4.0E-02	6.8E-05					1.7E-02	2.9E-05		
Baby Care	Diaper cream			2.6E+01	4.4E-02					2.6E+01	4.4E-02		
	Talc			8.0E-01	1.4E-03					8.0E-01	1.4E-03		
	Tissues			2.5E+00	4.3E-03					2.5E+00	4.3E-03		
Fragrance	Eau de toilette (spray) [a]	2.9E-02	5.9E-04	3.1E-01	5.3E-04			2.9E-02	5.9E-04	3.1E-01	5.3E-04		
	Eau de perfume (spray)	6.2E-03	1.2E-04	7.0E-02	1.2E-04			2.0E-03	4.0E-05	2.3E-02	3.9E-05		
Miscellaneous	Depilatory Cream			3.0E-02	5.1E-05					1.4E-03	2.4E-06		
	Massage Essential Oil			2.0E+01	3.3E-02					1.3E+00	2.2E-03		
	Bath Essential Oil			4.0E-02	6.8E-05					5.7E-03	9.7E-06		
Aggregate Exposure:		**38.4**	**0.8**	**614**	**1.0**	**4.1**	**4.1**	**10.8**	**0.2**	**307**	**0.5**	**4.1**	**4.1**
Aggregate Exposure excl. sun care products:		**15.4**	**0.3**	**374**	**0.6**	**4.1**	**4.1**	**8.5**	**0.2**	**282**	**0.5**	**4.1**	**4.1**

[a] - this product subcategory was selected amongst similarly shaded ones to calculate aggregate daily exposure

Table SI - 4. Results of the lower tier aggregate consumer exposure assessment to D5 from application of C&PCPs (evaporation scenario included)

Product category	Product subcategory	Acute exposure (i.e. on the day of use), mg/kg_bw/day						Chronic exposure, mg/kg_bw/day					
		Inhalation		Dermal		Oral		Inhalation		Dermal		Oral	
		external	internal	external	internal	external	internal	external	internal	external	internal	external	internal
Hair Care	Shampoo	1.8E-05	3.6E-07	2.1E-01	3.6E-04			6.5E-06	1.3E-07	7.5E-02	1.3E-04		
	Conditioner (rinse-off)	9.1E-06	1.8E-07	1.0E-01	1.8E-04			2.6E-06	5.2E-08	3.0E-02	5.1E-05		
	Conditioner (leave-on) [d]	2.2E-02	4.5E-04	5.2E+00	8.8E-03			6.4E-03	1.3E-04	1.5E+00	2.5E-03		
	Hair mask	5.7E-05	1.1E-06	2.6E-01	4.4E-04			1.6E-05	3.2E-07	7.4E-02	1.3E-04		
	Hair styling (wax, mousse, gel)	4.6E-02	9.3E-04	1.1E+01	1.8E-02			2.3E-02	4.6E-04	5.2E+00	8.8E-03		
	Fixative spray	9.2E+00	1.8E-01	8.0E-01	1.4E-03			5.5E+00	1.1E-01	4.8E-01	8.2E-04		
	Detangle spray	4.6E+00	9.2E-02	4.0E-01	6.8E-04			1.3E+00	2.6E-02	1.1E-01	1.9E-04		
	Semi-permanent dye	3.0E-04	6.0E-06	6.0E-01	1.0E-03			1.1E-05	2.1E-07	2.1E-02	3.6E-05		
	Permanent dye (oxidative)	3.3E-03	6.7E-05	2.0E+00	3.4E-03			9.1E-05	1.8E-06	5.5E-02	9.3E-05		
	Hair bleach [a]	5.9E-03	1.2E-04	2.7E+00	4.5E-03			1.6E-04	3.2E-06	7.3E-02	1.2E-04		
	Permanent wave	1.9E-03	3.8E-05	1.5E+00	2.5E-03			2.1E-05	4.2E-07	1.6E-02	2.8E-05		
Bath and Shower	Body wash (gel, cream, scrub)	8.6E-09	1.7E-10	2.5E-02	4.2E-05			3.9E-09	7.7E-11	1.1E-02	1.9E-05		
	Hand soap (liquid and solid)	8.0E-08	1.6E-09	2.7E-02	4.5E-05			8.0E-08	1.6E-09	2.7E-02	4.5E-05		
	Bath foam, oil, salt	8.2E-07	1.6E-08	1.7E-01	2.9E-04			2.3E-07	4.7E-09	4.8E-02	8.2E-05		
Body Care	Body lotion (cream, oil, milk)	1.3E-01	2.6E-03	9.4E+01	1.6E-01			1.3E-01	2.6E-03	9.4E+01	1.6E-01		
	Body pack (mud mask)	9.1E-06	1.8E-07	5.5E-01	9.4E-04			1.0E-07	2.0E-09	6.0E-03	1.0E-05		
Sun Care	Bronzer, sun-tan	3.2E-03	6.4E-05	1.0E+01	1.8E-02			3.4E-04	6.9E-06	1.1E+00	1.9E-03		
	Sun screen (cream, lotion)	5.1E-01	1.0E-02	1.9E+02	3.3E-01			5.2E-02	1.0E-03	2.0E+01	3.4E-02		
	Sun screen (spray) [a]	2.3E+01	4.6E-01	1.9E+02	3.3E-01			2.4E+00	4.7E-02	2.0E+01	3.4E-02		
Skin Care	Face cream (day, night)	1.5E-01	2.9E-03	1.8E+01	3.1E-02			1.5E-01	2.9E-03	1.8E+01	3.1E-02		
	Face whitening cream	7.3E-02	1.5E-03	9.2E+00	1.6E-02			1.8E-02	3.6E-04	2.3E+00	3.9E-03		

Product category	Product subcategory	Acute exposure (i.e. on the day of use), mg/kg_bw/day						Chronic exposure, mg/kg_bw/day					
		Inhalation		Dermal		Oral		Inhalation		Dermal		Oral	
		external	internal	external	internal	external	internal	external	internal	external	internal	external	internal
	Hand cream	1.9E-01	3.8E-03	2.6E+01	4.4E-02			1.9E-01	3.8E-03	2.6E+01	4.4E-02		
	Eye cream	1.3E-02	2.6E-04	1.6E+00	2.8E-03			1.3E-02	2.6E-04	1.6E+00	2.8E-03		
	Facial cleanser (peeling, scrub)	9.7E-10	1.9E-11	1.1E-03	1.8E-06			2.8E-10	5.6E-12	3.0E-04	5.2E-07		
	Facial cleanser (tissues)	1.5E-05	3.0E-07	1.3E-01	2.2E-04			4.3E-06	8.7E-08	3.7E-02	6.3E-05		
	Face pack (peel-off mask)	2.4E+00	4.9E-02	5.3E+01	9.1E-02			6.9E-01	1.4E-02	1.5E+01	2.6E-02		
Oral Care	Toothpaste					3.0E-02	3.0E-02					3.0E-02	3.0E-02
	Mouthwash					3.6E+00	3.6E+00					3.6E+00	3.6E+00
Foot Care	Antiperspirant (gel, cream)	1.9E-02	3.8E-04	9.6E+00	1.6E-02			1.9E-02	3.8E-04	9.6E+00	1.6E-02		
	Antifungal gel, cream	3.4E-04	6.9E-06	2.7E-01	4.6E-04			8.5E-05	1.7E-06	6.7E-02	1.1E-04		
Deodorant	Spray [a]	1.8E+00	3.5E-02	1.4E+01	2.4E-02			1.8E+00	3.5E-02	1.4E+01	2.4E-02		
	Stick and roll-on	2.5E-01	4.9E-03	1.0E+01	1.7E-02			1.2E-01	2.5E-03	5.0E+00	8.6E-03		
Shaving	Gel, foam	1.2E-06	2.4E-08	3.0E-02	5.1E-05			1.2E-06	2.4E-08	3.0E-02	5.1E-05		
	Balm, balsam	1.7E-02	3.4E-04	3.2E+00	5.4E-03			1.7E-02	3.4E-04	3.2E+00	5.4E-03		
Make-up	Mascara	2.1E-02	4.3E-04	2.7E-01	4.6E-04			2.1E-02	4.3E-04	2.7E-01	4.6E-04		
	Eye shadow (liquid and powder)	3.5E-04	7.0E-06	1.9E-01	3.2E-04			3.5E-04	7.0E-06	1.9E-01	3.2E-04		
	Eye liner	1.7E-04	3.4E-06	3.3E-02	5.7E-05			1.7E-04	3.4E-06	3.3E-02	5.7E-05		
	Liquid foundation	6.3E-03	1.3E-04	2.7E+00	4.6E-03			6.3E-03	1.3E-04	2.7E+00	4.6E-03		
	Compact powder	6.8E-03	1.4E-04	5.7E+00	9.6E-03			6.8E-03	1.4E-04	5.7E+00	9.6E-03		
	Remover	4.8E-05	9.5E-07	3.3E-01	5.6E-04			4.8E-05	9.5E-07	3.3E-01	5.6E-04		
	Lipstick, lip balm	1.5E-03	2.9E-05	3.5E-01	6.0E-04	4.3E-01	4.3E-01	1.5E-03	2.9E-05	3.5E-01	6.0E-04	4.3E-01	4.3E-01
Nail Care	Polish enamel, top and base coat	6.0E-06	1.2E-07	7.0E-03	1.2E-05			2.5E-06	5.1E-08	3.0E-03	5.1E-06		
	Polish remover	3.5E-05	7.0E-07	3.0E-02	5.1E-05			1.5E-05	3.0E-07	1.3E-02	2.2E-05		

Product category	Product subcategory	Acute exposure (i.e. on the day of use), mg/kg_bw/day						Chronic exposure, mg/kg_bw/day					
		Inhalation		Dermal		Oral		Inhalation		Dermal		Oral	
		external	internal	external	internal	external	internal	external	internal	external	internal	external	internal
Baby Care	Diaper cream	4.1E-02	8.1E-04	2.1E+01	3.5E-02			4.1E-02	8.1E-04	2.1E+01	3.5E-02		
	Talc	3.9E-05	7.7E-07	6.4E-01	1.1E-03			3.9E-05	7.7E-07	6.4E-01	1.1E-03		
	Tissues	4.5E-04	9.0E-06	2.0E+00	3.4E-03			4.5E-04	9.0E-06	2.0E+00	3.4E-03		
Fragrance	Eau de toilette (spray) [a]	2.9E-02	5.9E-04	2.4E-01	4.1E-04			2.9E-02	5.9E-04	2.4E-01	4.1E-04		
	Eau de perfume (spray)	6.2E-03	1.2E-04	5.0E-02	8.5E-05			2.0E-03	4.0E-05	1.6E-02	2.8E-05		
Miscellaneous	Depilatory Cream	4.2E-08	8.5E-10	2.0E-02	3.4E-05			2.0E-09	3.9E-11	9.3E-04	1.6E-06		
	Massage Essential Oil	7.2E-03	1.4E-04	1.6E+01	2.7E-02			4.8E-04	9.5E-06	1.0E+00	1.7E-03		
	Bath Essential Oil	3.0E-08	6.1E-10	3.0E-02	5.1E-05			4.3E-09	8.6E-11	4.3E-03	7.3E-06		
Aggregate Exposure:		**42.6**	**0.9**	**491**	**0.8**	**4.1**	**4.1**	**12.5**	**0.3**	**246**	**0.4**	**4.1**	**4.1**
Aggregate Exposure excl. sun care products:		**19.0**	**0.4**	**299**	**0.5**	**4.1**	**4.1**	**10.1**	**0.2**	**226**	**0.4**	**4.1**	**4.1**

[a] - this product subcategory was selected amongst similarly shaded ones to calculate aggregate daily exposure

2. Higher tier exposure assessment

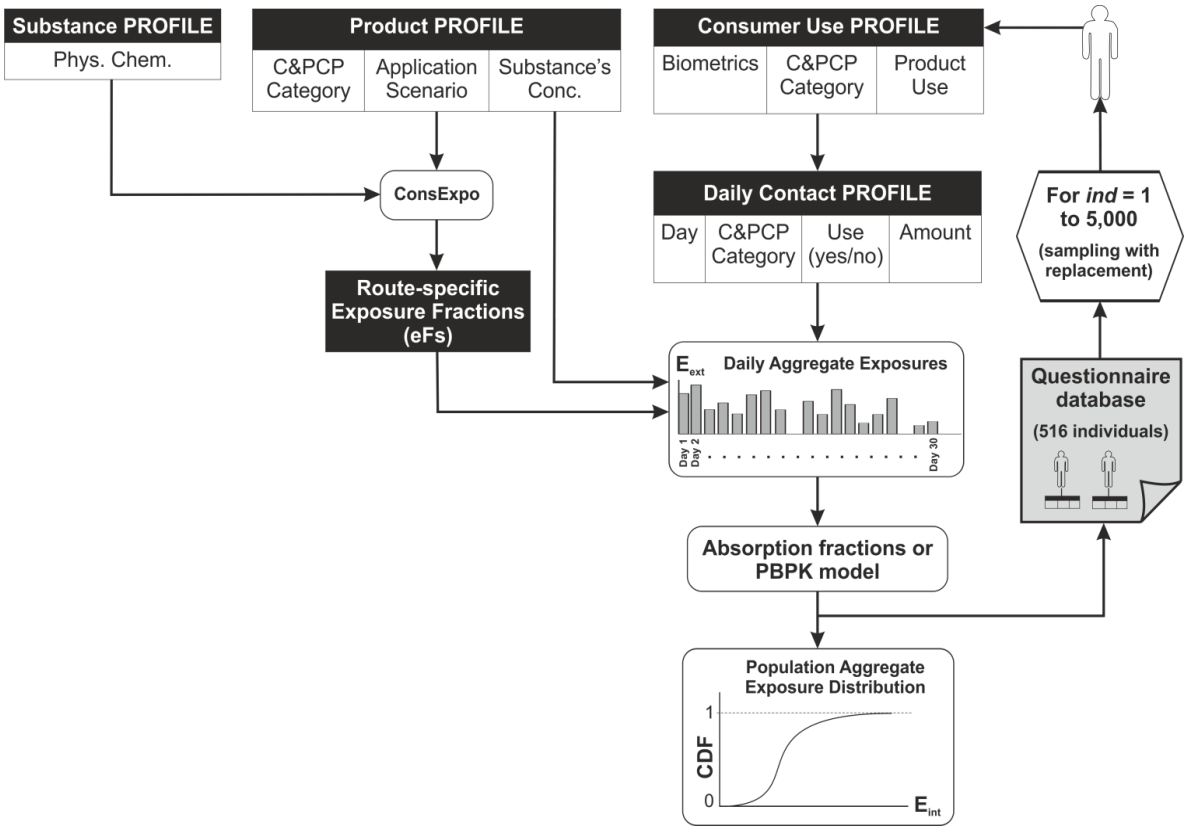

Figure SI-1. PACEM dataflow

The PACEM dataflow illustrated in Figure SI-1 can briefly be described with the following steps:

1. Generation of a simulated population of the required size (N=5,000 in this case-study) by repeated sampling from the questionnaire database containing consumer products use profiles for each individual in the survey population (n=516). The construction of a larger, simulated population allows for robust statistical and uncertainty analysis of the results;
2. Construction of the day-to-day contact profiles over the entire simulation period (30 days in this case study) for each individual in the simulated population. This is necessary, since the use frequencies in the questionnaire were acquired in the form of e.g. “once” or “twice” per week/month, therefore, the usage event has to be assigned to a specific day in the week/month. The first day of use was determined at random. Subsequent use of a product was determined by taking into account the preceding usage events and the specified use frequency of the respective individual. The use of different products is considered to be independent. The frequency of the product use per day is determined by drawing a random number from the corresponding individual distribution (where applicable). The product amount (per application) on the day of use is also determined by random sampling from individual amount distributions (where applicable). The time interval of 30 days was considered sufficient for modelling the individual day-to-day exposure profiles, because the C&PCPs appeared in the questionnaire can be used either daily (e.g. deodorant), weekly (e.g. nail polish, eye shadow) or monthly (e.g. sunscreen);
3. Calculation of single product exposures per 1 kg of body weight for every individual in the simulated population on each simulated day by multiplying the product use amounts and frequencies in the daily contact profile with chemical’s product concentrations and route-specific exposure fractions. The latter two factors, which are product specific, are determined by random sampling from corresponding parametric distributions (where applicable). Their descriptive summary is given in Table SI-5 and Table SI-8, respectively. Individual single product exposures are then aggregated route-wise into external daily exposures. Population aggregate exposure is built upon individual aggregate exposures.

Table SI - 5. Default application scenarios and weight fractions of D5 used in PACEM for different product categories

Product category	D5 weight fractions				Application scenario
	distribution type	parameter 1	parameter 2	parameter 3	
Aftershave_balsam	uniform	0.02	0.21	-	stay on skin
Aftershave_spray	uniform	0.02	0.21	-	spray on skin (perfume)
Aftersun_cream	triangular	0.003	0.88	0.0072	stay on skin
Bathing_foam	uniform	0.009	0.48	-	diluted in bath
Bathing_oil	uniform	0.009	0.48	-	diluted in bath
Bathing_both	uniform	0.009	0.48	-	diluted in bath
Bodylotion_milk	triangular	0.00192	0.88	0.0043	stay on skin
Bronzing_cream	uniform	0.01	0.24	-	stay on skin
Cleansing_lotion	uniform	0.03	0.59	-	rinse off skin
Conditioner_rinse	triangular	0.000013	0.89	0.0064	rinse off skin
Conditioner_leave	uniform	0.13	0.93	-	stay on hair
Conditioner_both	uniform	0.13	0.93	-	stay on hair
Deo_cream	triangular	0.18	0.63	0.356	stay on skin
Deo_roller_stick	triangular	0.00902	0.27	0.145	stay on skin
Deo_spray	triangular	0.00002	0.68	0.186	spray on skin (deodorant)
Deo_tissue	uniform	0.18	0.63	-	dermal wipe
Douchegel_foam_scrub	point	3.9e-07	-	-	rinse off skin
Eyepencil	point	0.22	-	-	stay on skin
Eyebrowpencil	uniform	0.13	0.51	-	stay on skin
Eyeshadow	uniform	0.03	0.72	-	stay on skin
Face_daycream	triangular	0.0029	0.61	0.3415	stay on skin
Face_nightcream	uniform	0.004	0.22	-	stay on skin
Hairfoam	point	0.00004	-	-	stay on hair
Hairgel	uniform	0.00004	0.0001	-	stay on hair
Hairlotion	uniform	0.13	0.93	-	stay on hair
Hairwax	uniform	0.13	0.93	-	stay on hair
Hairspray	uniform	0.0000067	0.36	-	spray on hair (hairspray)
Handcream	triangular	0.00054	0.88	0.0014	stay on skin
Lip balm	point	0.0000067	-	-	lip care
Lippencil	uniform	0.07	0.25	-	lip care
Lipstick	uniform	0.09	0.48	-	lip care
Liquid_foundation	triangular	0.021	0.83	0.0965	stay on skin
Makeup_remover	uniform	0.007	0.81	-	stay on skin
Mascara	uniform	0.0006	0.33	-	stay on skin
Nailpolish_feet	uniform	0.00009	0.00251	-	nail polish/remover
Nailpolish_hands	uniform	0.00009	0.00251	-	nail polish/remover
Nailpolish_both	uniform	0.00009	0.00251	-	nail polish/remover
Nailpolish_remover	uniform	0.03	0.04	-	nail polish/remover
Perfume_eaudetoilette_spray	uniform	0.27	0.41	-	spray on skin (perfume)
Rouge_powder	uniform	0.000001	0.3	-	stay on skin
Shampoo	point	0.00002	-	-	rinse off skin
Shavingfoam	point	0.04	-	-	rinse off skin
Shavinggel	point	0.04	-	-	rinse off skin
Shavingoil	point	0.04	-	-	rinse off skin
Shavingsoap	point	0.04	-	-	rinse off skin
Sunscreen_cream	triangular	0.001	0.49	0.364	stay on skin

Product category	D5 weight fractions				Application scenario
	distribution type	parameter 1	parameter 2	parameter 3	
Toothpaste	point	0.0000067	-	-	brush teeth

Table SI - 6. Product application scenarios linked to route-specific exposure fractions (eFs) in PACEM

Application scenario	eF_inhDIR	eF_inhINDIR	eF_dermDIR	eF_dermINDIR	eF_oral
stay on skin	-	eF1	eF2	eF2	-
rinse off skin	-	eF1	eF3	eF2	-
spray on skin (deodorant)	eF4	eF1	eF2	eF5	-
spray on skin (perfume)	eF16	eF1	eF2	eF5	-
spray on hair (hairspray)	eF15	eF1	eF10	eF5	-
stay on hair	-	eF1	eF10	eF2	-
diluted in bath	-	eF8	eF7	eF2	-
brush teeth	-	-	-	-	eF6
dermal wipe	-	eF1	eF9	eF2	-
nail polish/remover	-	eF12	eF11	eF2	-
lip care	-	-	eF10	eF2	eF13

eF=exposure fraction, inh=inhalation, derm=dermal exposure, oral= oral exposure, DIR= direct exposure, INDIR= indirect exposure

Table SI - 7. PACEM's equations for the calculation of route-specific exposures

Route exposure	Equation
direct inhalation exposure to sprays	$eF\_inhDIR \cdot (1 - eF\_dermINDIR) \cdot A$
indirect inhalation exposure to the material volatilized from skin	$eF\_inhINDIR \cdot eF\_dermINDIR \cdot eF\_dermDIR \cdot A$
direct dermal exposure	$(1 - eF\_inhINDIR) \cdot eF\_dermINDIR \cdot eF\_dermDIR \cdot A$
indirect dermal exposure (e.g. from hair spray)	0 (i.e. not calculated; needed as an intermediate value)
oral exposure	$eF\_oral \cdot A$

eF = exposure fraction, inh=inhalation, derm=dermal exposure, oral= oral exposure, DIR= direct exposure, INDIR= indirect exposure

A – amount of product used, g/event

Table SI - 8. Parameterization of route-specific exposure fractions (eFs) used in PACEM

eF	Application scenario	Distribution Type	Parameter 1[a]	Parameter 2[b]	Assumptions/Model	Notes
eF1	inh: evap from skin	beta	4.21	245.4	ConsExpo 5.0 evaporation model	
eF2	derm: stay on skin	point	1	-	worst-case	
eF3	derm: rinse off skin	point	0.01	-	1% of the product stays on skin after rinsing	
eF4	inh: deodorant sprayed to person	beta	4.85	529.3	ConsExpo 5.0 spray model	
eF5	derm: stay on hair	point	0.85	-	85%	
eF6	oral: brush teeth	uniform	0.1	0.3	reasonable worst-case	
eF7	derm: immerse in solution	uniform	0.001	0.01	accounting for dilution of the product	
eF8	inh: evap from solution	beta	3.17	149,221	ConsExpo 5.0 evaporation model	
eF9	derm: transfer wipe	uniform	0.01	0.2	from 1% to 20%	Gosens et al., 2013
eF10	derm: spray products or lip care	point	0.1	-	10%	see p.49-51 of RIVM Cosmetics Fact Sheet for details
eF11	derm: nail polish/remover	point	0.2	-	20% of product comes to direct contact with skin	
eF12	inh: nail polish/remover	beta	6.09	445.4	ConsExpo 5.0 evaporation model	
eF13	oral: lip care	point	0.9	-	worst-case	
eF15	inh: hairspray sprayed to person	beta	4.52	5,520	ConsExpo 5.0 spray model	
eF16	inh: perfumespray sprayed to person	beta	4.14	9,245	ConsExpo 5.0 spray model	

[a] – the parameter denotes either a point value, or the minimum in uniform distribution, or shape parameter α in beta distribution
[b] – the parameter denotes either a point value, or the maximum in uniform distribution, or shape parameter β in beta distribution

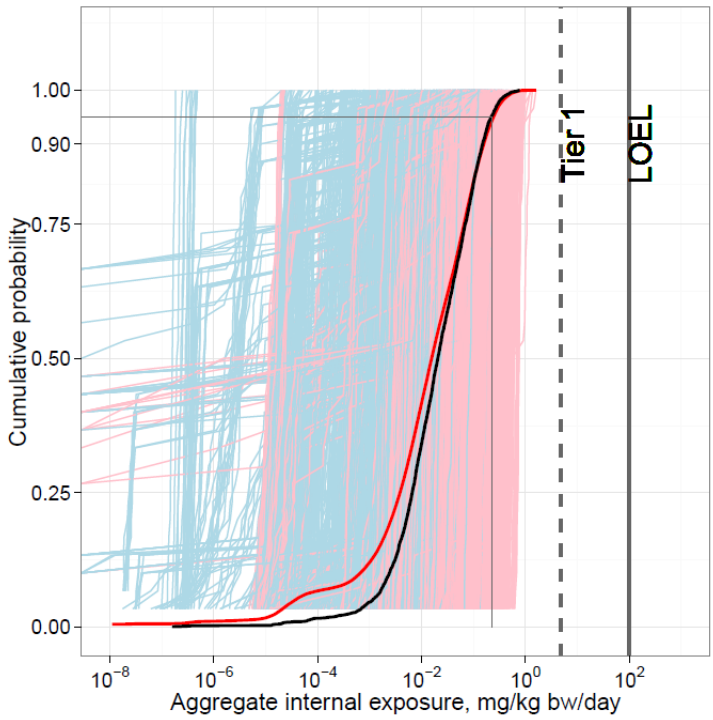

Figure SI-2. Cumulative probability plots illustrating on the y-axis the probability for an adult in a simulated population to be exposed and the corresponding internal exposure level on the x-axis. Thin coloured lines are the individual day-to-day aggregate exposure distributions (blue lines represent men; pink - women). Red and black solid curves are the cumulative distributions of the day-to-day acute and chronic aggregate internal exposure to D5 in the Dutch adult population, respectively.

3. Deriving MoE's for D5

In this paper we are not conducting a risk assessment. The derived MoE therefore should be considered only as a means to illustrate the risk assessment process and to highlight the achieved refinement when proceeding from a lower Tier to a higher Tier. For the MoE we are selecting the endpoint used by Canadian authorities in a risk assessment (Environment and Health Canada, 2008), but we are not evaluating it further.

The toxicity of D5 is relatively well studied ((SCCS) 2010, Johnson, Bergfeld et al. 2011). The NOAEL for reproductive toxicity of D5 in a 2-generation whole-body vapour inhalation study in rats was 160 ppm, i.e. the highest concentration that could be achieved without aerosol formation (Siddiqui, Stump et al. 2007). Reproductive parameters in the F0 and F1 generations were not affected by exposure to the test article. In a combined chronic toxicity and carcinogenicity whole-body vapour inhalation toxicity study, D5 induced uterine endometrial adenocarcinomas in female rats at 160 ppm (Dow Corning 2005) in addition to other non-neoplastic effects (e.g. liver weight increases) observed at 150 ppm. However, the relevance of this mode of action in humans is currently unclear. Therefore, the lack of genotoxic effects for D5 (based on limited genotoxicity data) suggests that the uterine tumours observed in the chronic carcinogenicity study could be due to threshold effects. The effects on the liver were also observed in subchronic toxicity studies in rats with either whole body vapour inhalation (Burns-Naas, Mast et al. 1998) or oral administration of D5 (Jäger 1991). The resulting oral LOEL (lowest observed adverse effect level) for liver weight increase in rats with oral dosing was 100 mg/kg bw/day when assuming 100% oral absorption. In other subchronic inhalation nose-only studies in rats, liver weight increases were reversible upon cessation of exposure (Burns-Naas, Mast et al. 1998). Dermal application of neat D5 up to 1600 mg D5/kg bw to rat skin for 28 days did not produce any test material related effects (Dow Corning, 1990). Overall, in the absence of reprotoxicity and carcinogenicity studies with oral dosing, it is not possible to infer whether the respective toxicological endpoints for D5 are independent of the route of exposure.

The results of the in-vitro tests with human skin (Jovanovic, McMahon et al. 2008) suggest that percutaneous absorption of D5 is very low or too slow to occur before volatilisation: following single dosage of applied neat or formulated D5 more than 91% of the substance volatilized before being absorbed. After 24 h only 0.04% of the applied dose was absorbed with the largest percentage remained in the skin. There

were no significant differences found in the absorption between neat and formulated D5. Low tendency to pass through the skin into systemic circulation was confirmed also in the in-vivo studies with both rats (0.17%) and humans (0.05%) (Dow Corning, 1996b, Plotzke et al., 2002 (Reddy, Looney et al. 2007, Jovanovic, McMahon et al. 2008). The retention of D5 following inhalation exposure was investigated in rats (Tobin, McNett et al. 2008). The reported values after single and multiple exposure range from 4-5% to 8-10% of the inhaled dose, respectively. Approximately 50-80% of this retained dose was attributed to the deposition on animals' fur. The kinetics of D5 in the human body after either inhalation or dermal absorption is somewhat similar and largely influenced by two specific processes: 1) high lipid partitioning leading to formation of a sequestered pool of D5 in the blood and 2) fast elimination of free D5 from blood due to exhalation. PBPK modelling (Reddy, Dobrev et al. 2008) showed that about 90% of the systemically absorbed D5 is exhaled unchanged within 24 hours. Note that the uptake after inhalation is much faster, suggesting that the inhalation exposure route will be of major concern. In addition, D5 is metabolized by hepatic clearance. The hydroxylated D5 (HO-D5) metabolite comprises about 1% of the systemic dose and is excreted with urine and feces. No metabolization of D5 was discovered in skin or in lung tissue.

Considering the preliminary information on the exposure sources and toxicologically relevant health endpoints of D5 collected in the tier 0, it is anticipated that the total systemic dose will primarily result from percutaneous absorption of D5 after dermal application of D5-containing C&PCPs and 'indirect' inhalation of D5 vapour volatilized from skin. 'Direct' inhalation exposure to D5 may also occur when using spray products. Finally, inadvertent ingestion of D5 contained in lip care products must be taken into account when calculating aggregate consumer exposure.

For the calculation of MoE we are therefore using the values of 100 mg/kg bw/day, which results in an MoE of 20 for the lower Tier. This MoE is normally considered not acceptable if based on a LOAEL.

4. Baseline excretion data for D5

Table SI - 9. The equivalent concentrations of free D5 in venous blood derived from the end-exhaled air samples for every baseline study volunteer

Volunteer ID (gender)	Use of D5-containing C&PCPs	End-exhaled air concentration of D5, ng/L		Free blood concentration of D5, ng/L		Timing of air sampling relative to the first exposure event, min
		1st sample	2nd sample	1st sample	2nd sample	
A (woman)	yes (deo-spray, face powder, hand cream)	2.94	3.43	1.20	1.41	1325
B (woman)	yes (deo-spray, body lotion, face cream, handcream)	9.21 [a]	3.94	3.78	1.62	1260
C (woman)	yes (deo-spray, day cream, leg balm)	23.21	13.25	9.52	5.43	1410
D (man)	no	1.35	1.76	0.55	0.72	73
E (man)	yes (shampoo, hair gel, body lotion)	2.01	1.71	0.82	0.70	1110
F (man)	yes (shampoo)	2.66	2.97	1.09	1.22	1095
G (man)	yes (deo-spray)	16.95	37.28	6.95	15.28	1575
H (woman)	yes (face night cream, handcream, day cream, lipstick)	3.67	1.86	1.50	0.76	780
I (woman)	yes (lipstick)	4.94 [a]	83.77	2.03	34.35	1440
J (woman)	yes (face cream, handcream)	<1.4 [a]	4.66	-	1.91	80
X (man)	no	3.22	<1.4	1.32	-	-
K (woman)	yes (deo-spray, shampoo, hair mousse)	10.38 [a]	55.86	4.26	22.90	360
Y (woman)	no	2.97	<1.4 [a]	1.22	-	-
L (woman)	yes (deo-spray, body lotion, handcream, face cream, shampoo, conditioner)	6.82	2.09	2.80	0.86	910
M (woman)	yes (day cream, skin care oil)	34.13	1.62 [a]	13.99	0.66	1380

[a] - Note that there is a rather large difference between the two samples collected. The lowest value most probably does not represent D5 concentration in alveolar air, as the volunteer may not have exhaled completely. It rather represents D5 concentration in air that consists of a combination of air present in the death space of the lungs and in the alveoli.

Table SI - 10. Use of D5 containing products reported by individual baseline study volunteers

Volunteer ID	Body weight, kg	Age, years	Applied product category	Timing of exposure relative to the first exposure event, min	D5 product concentration, mg/g			Applied amount, g			Surface area of application, cm^2
					med	min	max	med	min	max	
A	60	23	Handcream	0	10.4	1.6	19.1	0.7	0.5	0.8	669
			Rouge_powder	1060	150.0	0.001	300.0	0.008	0.007	0.01	753
			Deo_spray	1070	223.7	53.3	394.1	0.356	0.319	0.412	167
B	71	26	Handcream	0	10.4	1.6	19.1	0.2	0.1	0.3	745
			Bodylotion_milk	300	26.0	3.9	48.1	8.9	7.2	13	10,061
			Deo_spray	960	223.7	53.3	394.1	0.356	0.319	0.412	186
			Face_daycream	960	115.2	16.3	214.1	0.2	0.1	0.3	838
C	65	64	Deo_spray	0	223.7	53.3	394.1	0.356	0.319	0.412	174
			Leg_balm	10	26.0	3.9	48.1	5.6	3.9	7.2	6,270
			Face_daycream	20	115.2	16.3	214.1	0.2	0.1	0.3	958
			Deo_spray	1270	223.7	53.3	394.1	0.356	0.319	0.412	174
			Leg_balm	1278	26.0	3.9	48.1	5.6	3.9	7.2	6,270
			Face_daycream	1320	115.2	16.3	214.1	0.2	0.1	0.3	958
D	70	56	Eyeliner	0	150.5	1	300	0.0023	0.002	0.003	9
E	75	64	Shampoo	0	80.0	10	150	7.7	6.5	8.9	883
			Hairgel	0	125.5	1	250	3.8	2.8	4.8	883
			Bodylotion_milk	0	26.0	3.9	48.1	8.9	7.2	13	17,669
			Hairgel	690	125.5	1	250	3.8	2.8	4.8	883
F	75	21	Shampoo	0	80.0	10	150	5.2	4	6.5	879
G	86	55	Deo_spray	0	223.7	53.3	394.1	0.356	0.319	0.412	210
			Deo_spray	1485	223.7	53.3	394.1	0.356	0.319	0.412	210
H	64	70	Face_nightcream	0	115.2	16.3	214.1	0.9	0.8	1.1	778
			Handcream	0	10.4	1.6	19.1	0.9	0.8	1.1	691

Volunteer ID	Body weight, kg	Age, years	Applied product category	Timing of exposure relative to the first exposure event, min	D5 product concentration, mg/g			Applied amount, g			Surface area of application, cm^2
					med	min	max	med	min	max	
			Mascara	1180	100.5	1	200	0.01193	0.0106	0.0142	8
J	69	22	Face_daycream	0	115.2	16.3	214.1	0.2	0.1	0.3	817
			Handcream	45	10.4	1.6	19.1	0.4	0.4	0.5	726
K	46	25	Shampoo	0	80.0	10	150	2.7	1.4	4	643
			Deo_spray	12	223.7	53.3	394.1	0.356	0.319	0.412	143
			Hairfoam	15	0.04	0.04	0.04	3	2.5	3.5	643
L	83	43	Bodylotion_milk	0	26.0	3.9	48.1	1.8	1.4	2.1	1,105
			Handcream	10	10.4	1.6	19.1	0.9	0.8	1.1	904
			Shampoo	416	80.0	10	150	5.2	4	6.5	904
			Conditioner_rinse	420	8.1	0.023	16.2	7.7	6.5	8.9	904
			Bodylotion_milk	446	26.0	3.9	48.1	1.8	1.4	2.1	1,105
			Deo_spray	445	223.7	53.3	394.1	0.356	0.319	0.412	201
			Eye_cream	447	115.2	16.3	214.1	0.1	0.1	0.1	10
			Handcream	450	10.4	1.6	19.1	0.9	0.8	1.1	904
M	73	21	Face_daycream	0	115.2	16.3	214.1	0.45	0.4	0.5	840
			Face_daycream	720	115.2	16.3	214.1	0.45	0.4	0.5	840

5. Modelling indoor air concentrations of D5

The occurrence of D5 in the indoor environment should reflect the consumer use of D5-containing C&PCPs (Hodgson et al., 2003; Maddalena et al., 2011). In order to verify the consumer use data and the modelling assumptions employed in PACEM we attempted to predict D5 concentrations in indoor air and evaluate the modelling results in relation to existing measurement data. The main test data were from (Pieri et al., 2013), in which 91 air samples were collected from eight types of indoor residential environments in the UK and Italy and analyzed for presence of linear and cyclic siloxanes using thermal desorption gas chromatography coupled with mass spectrometry (TD-GC/MS). The sampling protocol required the windows and doors being kept closed at least for 8 hours prior to the air sampling event. The most abundant cVMS found indoors was D5, with average concentrations ranging from 7.5 to 170 $\mu g/m^3$ in the samples from Italy and 45-270 $\mu g/m^3$ in indoor environments in the UK. The variability of D5 air concentrations among different room types was significant for both countries. Elevated residential concentrations of D5 were typically observed in bathrooms, adults' rooms and children's bedrooms.

Time-dependent indoor air concentrations were modelled using the PACEM's output of aggregate consumer exposure as a starting point. For every individual in the PACEM population the amounts of D5-containing C&PCPs applied daily either dermally or in sprays were fed into a simple mechanistic box model to simulate the fate of D5 in the indoor environment. The exposure-related parameters assumed in the model were similar to those encountered for the development of inhalation exposure fractions in PACEM, namely: 1) D5 is instantly applied in the pure form; 2) aggregated application of C&PCPs occurs in a room volume of $U(2; 10)$ m^3 with the ventilation rate of $U(1; 5)$ times/hour; 3) skin temperature is 32ºC (relevant for volatilization of D5 from skin); 4) the room air is well mixed at all times. The fate model comprises the "evaporation" and the "spraying" modules, both copying the corresponding equations implemented in ConsExpo 4.0 consumer exposure assessment tool (Delmaar et al., 2005).

The evaporation module explicitly models the release of D5 from the treated skin surface area by evaporation. Volatilization of the compound from a thin liquid film formed on the skin after product application is described with a set of coupled differential equations accounting for the time-dependent mass balance of D5 remained in the source, evaporated into the air and subsequently being removed by the ventilation. The rate of evaporation depends on the volatility of the liquid (vapour pressure or boiling point), the dimensions of the source (surface

area), and the environmental conditions, such as air temperature, air velocity, direction, and turbulence. The vapour pressure of pure D5 at room temperature is readily available (i.e. 33.2 Pa) and the vapour pressure at other temperatures can be assessed using, for example Clausius-Clapeyron equation (assuming that between 290 K and the boiling point temperature the change in the enthalpy of vaporization is linearly related to temperature):

$$ln\left(\frac{P}{P_0}\right) = \frac{\Delta H}{R}\left(\frac{1}{T_0} - \frac{1}{T}\right) \qquad \text{eq. SI-1}$$

where

P – is the vapour pressure (Pa)

P_0 – vapor pressure (Pa) at a known temperature T_0 (K)

ΔH – enthalpy of vaporization (J/mol) at actual temperature T (K)

R – the ideal gas law constant (J/K/mol)

T – the actual temperature (in K)

Following the explanations given in (Gajjar et al., 2013), on the basis of mass transfer theory, the specific evaporation rate R_{ii} of a pure liquid (mol/m^2/s) can be expressed as:

$$R_{ii} = k_{ii}(C_{ii} - C_i) \cong k_{ii}C_{ii} = k_{ii}\frac{p_{ii}}{RT} \qquad \text{eq. SI-2}$$

where

k_{ii} – the gas-phase mass transfer coefficient (m/s)

C_{ii} – the air concentration of substance *i* in equilibrium with pure liquid *i* (mol/m^3)

C_i – the air concentration of substance *i* in the room (mol/m^3)

p_{ii} – the vapor pressure of substance *i* (Pa) at actual temperature T (K)

R – the gas constant (Pa·m^3/mol/K)

T – the actual temperature (K)

Under most circumstances, $C_i << C_{ii}$, so that C_i can be neglected (Olsen et al., 1992), except for a few extreme situations with very large evaporation surface areas and low ventilation rates (Jayjock, 2003).

The spraying module calculates an incremental mass of D5 vapour in the air by accounting for continuous evaporation of aerosols generated during spraying (e.g. application of a deodorant-antiperspirant, hair spray). A certain fraction of the initially sprayed product ends up on consumer's skin and thereafter is excluded from the

overall mass balance. The released aerosols/droplets are described with the initial size-distributions, which were shown to be strongly product-type dependent (Delmaar and Bremmer, 2009). The corresponding droplet size distributions relevant for eF4, eF15 and eF16 inhalation exposure fractions (Table SI-8) were taken from (Delmaar and Bremmer, 2009). The module also considers droplets' deposition due to gravitational settling in the earth's gravity field. The deposition is characterized by the diameter-dependent Stokes settling velocity, $v_s(d_p)$:

$$v_s(d_p) = \frac{\rho g}{18\mu} d_p^2 S \qquad \text{eq. SI-3}$$

where

- $v_s(d_p)$ – Stokes settling velocity of the droplet with diameter d_p (m/s)
- d_p – droplet/particle diameter (m)
- μ – dynamic air viscosity (kg/m/s)
- ρ – mass density of aerosol (kg/m^3)
- g – acceleration due to gravity (m/s^2)
- S – the correction factor (either slip correction or coefficient of drag). For droplets with d_p<50 µm falling in laminar flow (with Re<1.0) S=1, i.e. no correction necessary (Hinds, 1982).

The changing droplet diameter due to evaporation makes the settling velocity a time dependent quantity decreasing with increasing residence time. Preliminary analysis revealed that, e.g. 1000 mg of D5 released in an initial droplet size lognormal distribution with P50 = 8.3 and CV = 0.84 will evaporate into the air within the first two to three minutes (Figure SI-2). Smaller masses will evaporate even faster. Therefore, for simplification we assumed that pure liquid D5 released in droplets will transition into the gas phase immediately. This assumption should not affect significantly the final results of the modelled D5 concentrations in indoor air.

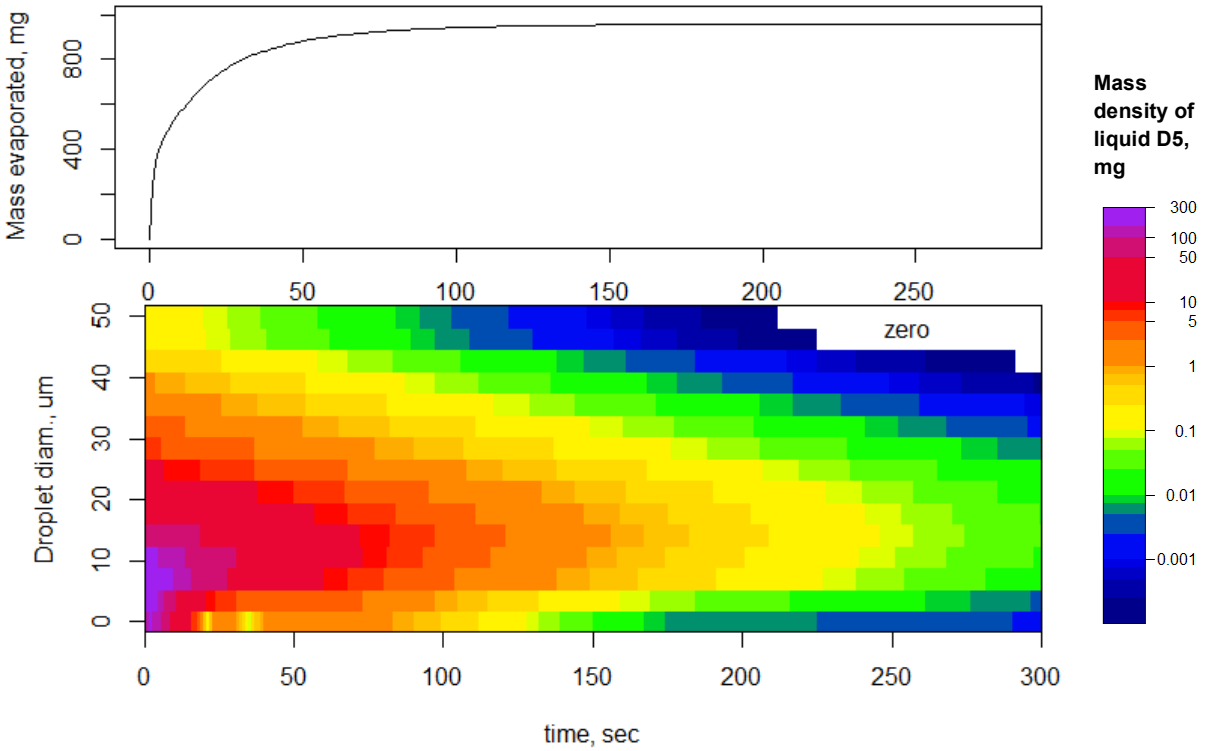

Figure SI - 3. Time evolution of liquid D5 mass (1000 mg) depending on the droplet diameter (lower panel). Mass of D5 transitioned into vapour is also shown (upper panel). The simulations were carried in R (R Development Core Team, 2010) on the basis of the equations shown above.

6. Uncertainty analysis

Table SI - 11. Qualitative characterization of uncertainty and variability for the exposure factors in PACEM

Exposure factor	Type	Uncertainty	Variability
consumers' body weight	Variable (V)	source: uncertainty in the estimation handling: considered small (self-reported values)	source: natural inter-individual variability handling: individual values for every person in the simulated population
product amounts reported by consumers / questionnaire respondents	Uncertain and variable (UV)	source: uncertainty in the estimation by photographs plus the measurement error while weighting the product amounts handling: uniform distributions assigned to each simulated individual from the questionnaire	source: natural inter-individual variability handling: point values drawn from the individual distributions for every person in the simulated population
product use frequencies reported by consumers / questionnaire respondents	Uncertain and variable (UV)	source: uncertainty associated with imprecise answers specified in broad ranges (e.g. 2-3 times per week) handling: uniform distributions assigned to each simulated individual from the questionnaire	source: natural inter-individual variability handling: point values drawn from the individual distributions for every person in the simulated population
market share of D5-containing products	-	source: uncertainty in the estimation handling: not included	source: spatial and temporal variability among product categories handling: not included
product weight fractions	Uncertain and variable (UV)	source: measurement error handling: considered small	source: variability among different product brands handling: parametric distributions assigned to each product category in the model
exposure fractions	Uncertain and variable (UV)	source: uncertainty associated with the input parameters used to calculate exposure fractions plus the uncertainty from fitting handling: considered small	source: natural inter-individual variability handling: uniform or beta distributions assigned to corresponding exposure scenarios in the model (see SI)
route specific absorption factors	Uncertain and variable (UV)	source: uncertainty in the estimation based on the data from animal studies and experiments with human volunteers handling: considered small	source: natural inter-individual variability. For dermal absorption within-individual variation depending on the body part exposed handling: considered small

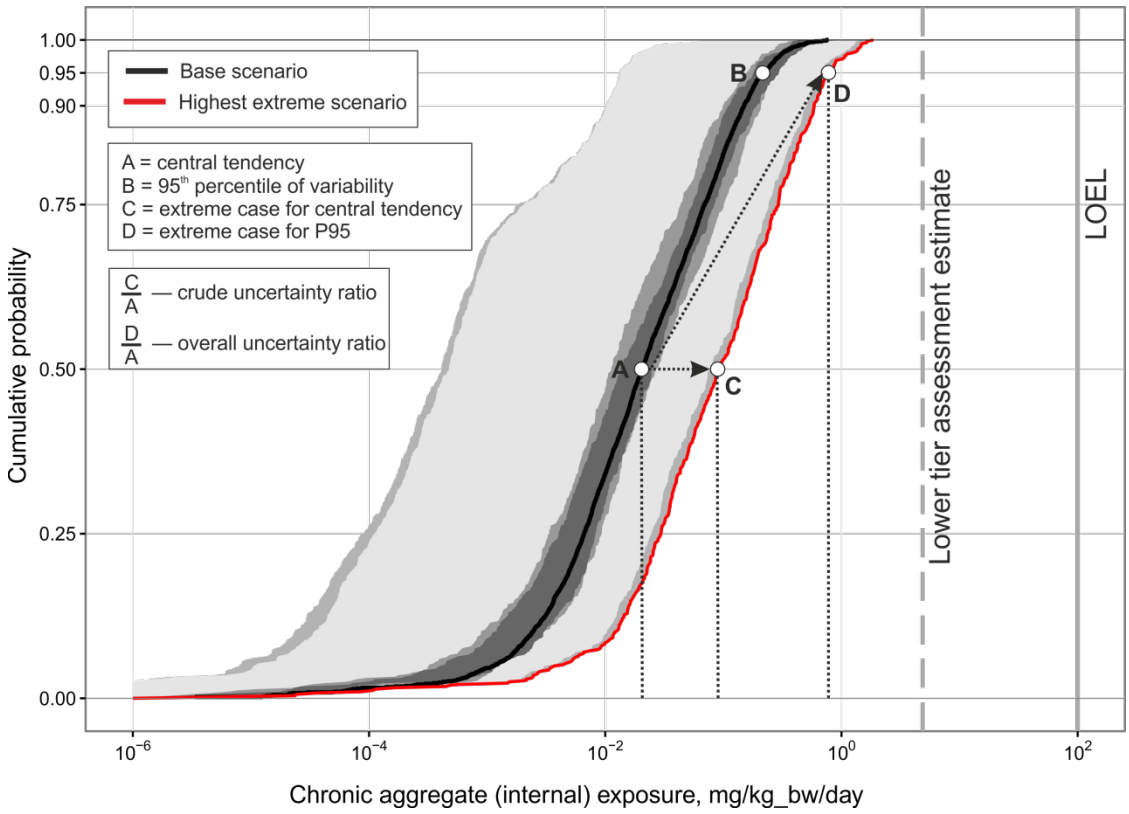

Figure SI - 4. The uncertainty ranges for median (black curve) aggregate consumer exposure to D5 in Dutch adult population. The darkest shaded area around the median curve represents the maximum uncertainty associated with the reported product use amounts; the surrounding lighter region illustrates the same value for both the amounts and use frequencies considered together; the lightest area comprise in addition the uncertainty from estimated D5 weight fractions; the outermost margins include all the uncertain parameters modelled in one run, i.e. use amounts, application frequencies, D5 product concentrations and the route-specific exposure fractions. The red curve represents the upper limit of the uncertainty range.

7. Variance-based global sensitivity analysis (GSA)

The first order and the total Sobol's sensitivity indices for the higher tier model inputs were calculated (Table SI-12) based on the 100,000 population sample reconstructed from the survey population, following the approach as described elsewhere (Jansen, 1999; Saltelli et al., 2010). The first order sensitivity indices measure only the contribution of the main effect of the input variable, whereas the total index is a summary sensitivity measure inclusive of interactions effect of any order (Homma and Saltelli, 1996; Sobol, 2001). The interaction effect between the two inputs represents part of the output variance that cannot be explained by the sum of the individual main effects of these two inputs (Saltelli et al., 2000). Therefore, the total index accounts for all possible (synergistic) terms between the given parameter and all the others. The adopted GSA method performs well regardless of the model's linearity and monotonicity assumptions.

Sensitivity indices in Table SI-12 represent a measure of the importance of a particular exposure parameter for the population internal exposure stemming from a certain product. The fact that the total indices are typically higher than the corresponding first-order indices indicates that the input parameters will interact and therefore will have a higher impact on the output uncertainty. Considering the example of a body lotion, the sum of the first-order indices for females equals to 0.53, with the use amount, use frequency and D5 concentration sharing almost equally the total contribution. Still 47% of the output variance is explained by interactions of input variances (and uncertainties). For men the variation of the amount factor is more pronounced, leading to the nearly two-fold increase of its contribution when compared to other parameters. Interestingly, the total variance of D5 exposure from lipstick is mostly governed by the variation of the use frequency parameter. Overall, the variance of the body weight and the route-specific exposure fractions (data not shown) exhibit almost no direct influence on the output metric for any C&PCP. Finally, the first-order indices above one designate the C&PCP categories, for which the empirical cumulative distribution functions of the input variables have prominent steps. Zero valued indices occur in the case the input parameter per se has zero variance (e.g. the constructed user population consists of the same individual). For such factors larger population size is required to enhance the input data.

Table SI - 12. Sobol's first-order sensitivity indices (first SI) and total sensitivity indices (total SI) for the main C&PCP categories contributing to the aggregate consumer internal exposure of D5 calculated with PACEM

Product	Women									Men								
	N	body weight		use amount		use frequency		D5 concentration		N	body weight		use amount		use frequency		D5 concentration	
		first SI	total SI	first SI	total SI	first SI	total SI	first SI	total SI		first SI	total SI	first SI	total SI	first SI	total SI	first SI	total SI
Aftershave balsam	3,067	0.011	0.027	0.456	0.829	0.243	0.600	0.125	0.288	13,797	0.015	0.033	0.437	0.929	0.393	0.845	0.169	0.319
Aftershave spray	1,509	0.024	0.038	0.185	0.280	0.268	0.381	0.249	0.394	8,443	0.020	0.041	0.123	0.202	0.389	0.533	0.241	0.383
Aftersun cream	28,668	0.003	0.019	0.097	0.353	0.170	0.474	0.070	0.380	14,957	0.002	0.015	0.123	0.606	0.269	0.774	0.068	0.350
Body lotion	40,980	0.009	0.036	0.164	0.405	0.189	0.436	0.171	0.451	8,784	0.003	0.025	0.209	0.570	0.110	0.423	0.100	0.408
Deo roller/stick	24,519	0.011	0.038	0.506	0.709	0.110	0.264	0.062	0.179	15,316	0.023	0.058	0.610	1.167	0.362	0.748	0.162	0.277
Deo spray	31,989	0.011	0.030	0.452	0.745	0.159	0.354	0.120	0.304	22,119	0.015	0.039	0.560	1.649	0.292	0.643	0.172	0.342
Face cream	72,307	0.016	0.036	0.154	0.293	0.131	0.258	0.366	0.550	5,557	0.011	0.041	0.185	0.412	0.224	0.490	0.214	0.432
Hair spray	25,706	0.004	0.029	0.186	0.472	0.175	0.479	0.063	0.306	4,304	0.005	0.012	0.288	1.156	0.506	1.603	0.186	0.378
Handcream	40,158	0.007	0.030	0.065	0.229	0.306	0.614	0.147	0.421	11,233	0.003	0.021	0.056	0.265	0.531	1.066	0.098	0.396
Lipstick	32,314	0.013	0.039	0.047	0.110	0.596	0.765	0.088	0.209	796	0.001	0.006	0.001	0.001	0.895	1.057	0.064	0.202
Liquid foundation	17,871	0.013	0.040	0.218	0.445	0.321	0.617	0.192	0.393	197	0.000	0.000	0.247	0.517	0.246	0.500	0.323	0.513
Makeup remover	22,797	0.016	0.043	0.365	0.576	0.082	0.189	0.199	0.390	197	0.000	0.000	0.091	0.160	0.432	0.570	0.365	0.503
Perfume spray	45,331	0.032	0.062	0.167	0.256	0.543	0.656	0.016	0.030	16,865	0.012	0.026	0.151	0.270	0.404	0.532	0.010	0.024
Sunscreen cream	45,502	0.005	0.028	0.093	0.465	0.274	0.700	0.067	0.317	24,192	0.002	0.014	0.185	0.832	0.358	1.041	0.083	0.341
Toothpaste	55,347	0.059	0.084	0.478	0.580	0.168	0.232	0.000	0.000	32,090	0.037	0.056	0.436	0.532	0.239	0.312	0.000	0.000

8. References

Biesterbos, J.W.H., Dudzina, T., Delmaar, C.J., Bakker, M.I., Russel, F.G., von Goetz, N., Scheepers, P.T., Roeleveld, N., 2013. Usage patterns of personal care products: important factors for exposure assessment. Food Chem Toxicol 55, 8-17.

Bremmer, H.J., Prud'Homme de Lodder, L.C.H., van Engelen, J.G.M., 2006a. General Fact Sheet. Limiting conditions and reliability, ventilation, room size, body surface area. Updated version for ConsExpo 4. RIVM.

Bremmer, H.J., Prud'homme de Lodder, L,C.H., van Engelen, J.G.M. , 2006b. Cosmetics Fact Sheet To assess the risks for the consumer. Updated version for ConsExpo 4. RIVM.

Delmaar, C.J., Bremmer, H.J., 2009. The ConsExpo Spray Model. Modeling and experimental validation fo the inhalation exposure of consumers to aerosols from spray cans and trigger sprays. National Institute for Public Health and the Environment (RIVM).

Delmaar, J.E., Park, M.V.D.Z., van Engelen, J.G.M., 2005. ConsExpo 4.0 Consumer Exposure and Uptake Models. Program Manual. RIVM.

Environment and Health Canada, 2008. Screening assessment for the challenge. Decamethylcyclopentasiloxane (D5).

European Chemicals Agency (ECHA), 2012. Guidance on information requirements and chemical safety assessment. Chapter R.15: Consumer exposure estimation.

European Commission (EC), 2013. Regulation (EC) No 1223/2009 (Article 13). Cosmetic Products Notification Portal (CPNP) User Manual., in: Commission, E. (Ed.). Cosmetic Europe.

Gajjar, R.M., Miller, M.A., Kasting, G.B., 2013. Evaporation of volatile organic compounds from human skin in vitro. Ann Occup Hyg 57, 853-865.

Hall, B., Steiling, W., Safford, B., Coroama, M., Tozer, S., Firmani, C., McNamara, C., Gibney, M., 2011. European consumer exposure to cosmetic products, a framework for conducting population exposure assessments Part 2. Food and Chemical Toxicology 49, 408-422.

Hall, B., Tozer, S., Safford, B., Coroama, M., Steiling, W., Leneveu-Duchemin, M.C., McNamara, C., Gibney, M., 2007. European consumer exposure to cosmetic products, a framework for conducting population exposure assessments. Food and Chemical Toxicology 45, 2097-2108.

Hinds, W.C., 1982. Aerosol Technology: Properties, Behavior, and Measurement of Airborne Particles, 2nd ed. Wiley & Sons.

Hodgson, A.T., Faulkner, D., Sullivan, D.P., DiBartolomeo, D.L., Russell, M.L., Fisk, W.J., 2003. Effect of outside air ventilation rate on volatile organic compound concentrations in a call center. Atmospheric Environment 37, 5517-5527.

Homma, T., Saltelli, A., 1996. Importance measures in global sensitivity analysis of nonlinear models. Reliability Engineering & System Safety 52, 1-17.

Jansen, M.J.W., 1999. Analysis of variance designs for model output. Computer Physics Communications 117, 35-43.

Jayjock, M.A., 2003. Modeling Inhalation Exposure. Nature Publishing Group.

Maddalena, R., McKone, T., Destaillats, H., Rusell, M., Hodgson, A., Perino, C., 2011. Quantifying Pollutant Emissions from Office Equipment: A Concern in Energy-Efficient Buildings. California Energy Commission, PIER Energy-Related Environmental Research.

McNamara, C., Rohan, D., Golden, D., Gibney, M., Hall, B., Tozer, S., Safford, B., Coroama, M., Leneveu-Duchemin, M.C., Steiling, W., 2007. Probabilistic modelling of European consumer exposure to cosmetic products. Food and Chemical Toxicology 45, 2086-2096.

Olsen, E., Olsen, I.B., Wallstrom, E.V.A., Rasmussen, D., 1992. On the substitution of chemicals - use of the SUBFAC-index for volatile substances. Annals of Occupational Hygiene 36, 637-652.

Pieri, F., Katsoyiannis, A., Martellini, T., Hughes, D., Jones, K.C., Cincinelli, A., 2013. Occurrence of linear and cyclic volatile methyl siloxanes in indoor air samples (UK and Italy) and their isotopic characterization. Environ Int 59, 363-371.

R Development Core Team, 2010. R. A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.

Saltelli, A., Annoni, P., Azzini, I., Campolongo, F., Ratto, M., Tarantola, S., 2010. Variance based sensitivity analysis of model output. Design and estimator for the total sensitivity index. Computer Physics Communications 181, 259-270.

Saltelli, A., Chan, K., Scott, E.M., 2000. Sensitivity Analysis. Wiley & Sons, Chichester.

Scientific committee on consumer safety (SCCS), 2012. The SCCS's notes of guidance for the testing of cosmetic ingredients and their safety evaluation. 8th revision. European Commission (EC).

Sobol, I.M., 2001. Global sensitivity indices for nonlinear mathematical models and their Monte Carlo estimates. Mathematics and Computers in Simulation 55, 271-280.