Supporting Information

Contribution of direct and indirect exposure to human serum concentrations of PFOA in an occupationally exposed group of ski waxers

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Appendix 1. Glossary of model variables with units

B_w: Body weight [kg]

$C_{airFTOH}$: Concentration of 8:2 FTOH in air (gas phase) [ng/m^3]

$C_{airPFOA}$: Concentration of PFOA in air (gas phase) [ng/m^3]

D_{bkg}: Average daily intake of PFOA in the general population [ng/kg/d]

C_{PFOA}: Concentration of PFOA in serum [ng/ml]

C_{dust}: Concentration of suspended dust particles in the cabin [mg/m^3]

C_{dPFOA}: Concentration of PFOA sorbed to suspended dust [ng/mg dust]

E_i: Absorption efficiency of PFOA/8:2 FTOH through the respiratory epithelium [unitless]

E_{gi}: Absorption efficiency of PFOA sorbed to suspended dust through the gastro-intestinal epithelium [unitless]

I_{direct}: Intake of PFOA from direct exposure [ng/week]

$I_{indirect}$: Intake of PFOA from indirect exposure [ng/week]

I_{bkg}: Intake of background PFOA [ng/week]

k_e: Internal Elimination rate of PFOA [/week]

K_i: Air inhalation rate [m^3/hour]

$t_{1/2:}$ Elimination half-life of PFOA in the human body [years]

V_d: Volume of distribution of PFOA [ml/kg]

W_h: hours of exposure per week [h/week]

Y_{meta}: Metabolism yield [unitless]

Appendix 2. Information on the ski wax technicians and time frame of Nilsson et al.'s occupational study[1,2]

Table A2-1. Information on the six ski wax technicians

Technician #[a]	Years as technician	Weight (kg)	Age	Team 1st season	Team 2nd season	Occupation during unexposed period
1	3	86	27	Sweden	Sweden	student
2	6	67	51	Sweden	Sweden	carpenter
3	6	87	33	Sweden	Sweden	full time technician
4	10	80	38	Sweden	Sweden	gardener
6	15	81	45	USA	Sweden	carpenter
8	12	81	45	USA	Sweden	engineer

[a]the numbers correspond to the initial listing in Nilsson et al.[1,2]

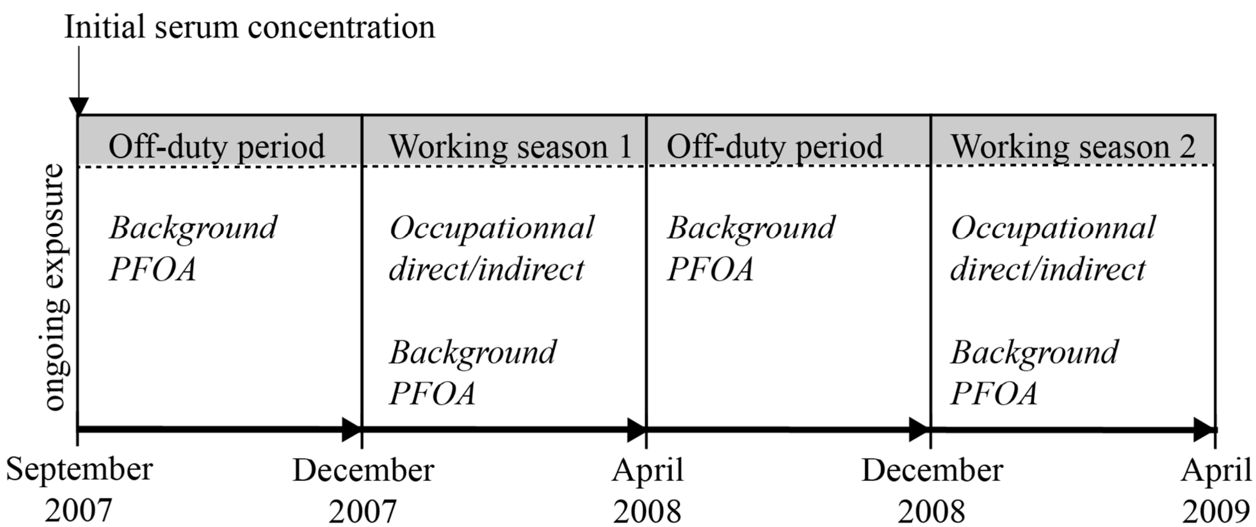


Figure A2-1. *Time frame of Nilsson et al.'s study[1,2] on the ski wax technicians. The sampling campaign covers two working seasons, during which both background and occupational exposure occurred and there were two off-duty periods, during which technicians' exposure to PFOA was reduced to background levels.*

Appendix 3. Treatment of the external exposure data for the model fitting (i.e. concentration of suspended dust particles (C_{dust}, in mg/m^3), concentration of PFOA sorbed to suspended dust (C_{dPFOA}, in ng/mg dust), concentration of PFOA in air ($C_{airPFOA}$, in ng/m^3) and concentration of 8:2 FTOH in air ($C_{airFTOH}$, in ng/m^3))

As briefly described in section 2.3.1 of the manuscript, samples of air and dust were collected once a month, whenever cross-country ski competitions were taking place. Two active sampling methods were used: 1) a personal pump was installed on each technician close to the breathing zone; 2) a stationary high volume sampler was placed on a platform in the cabin. Since exposure increased nearer the source (i.e. the waxing material) and each technician was using different wax products, C_{dust} (in mg/m^3), C_{dPFOA} (in ng/mg dust), $C_{airPFOA}$ (in ng/m^3) and $C_{airFTOH}$ (in ng/m^3) were taken from the personal pump measurements of the corresponding technician. When such data were not available, the averaged measurements obtained with the platform pump were used. In some rare cases, neither personal nor platform pump measurements were available within a given month. To circumvent this lack of data, the averaged measurement calculated from the personal pump data of the other technicians for the month of interest was used. Finally, because no sampling was carried out in February 2009, the external exposure data obtained in January 2009 were used for that month. For the four-year simulation, external exposure data were available for the month of March 2010 only. Therefore, it was assumed that the external exposure was the same throughout the working seasons of 2010 and 2011 and input data were extrapolated from the single external exposure concentration. A summary of the type of input data used in the model is provided for each technician in Table A3-1.

Except for a few exceptions, the concentrations were only measured one day per month. As a consequence, the external exposure parameters for each week were extrapolated from the single measurement of the corresponding month.

Table A3-1: *Type of data used as external exposure parameters for each technician. "Personal" and "platform" refer to the data that were obtained from the personal and platform pumps, respectively. "Average" indicates the month for which no data were available and where the exposure value was extrapolated from the averaged personal pump measurements of the other technicians for the same month.*

Technician #	1	2	3	4	6	8
Input data used for suspended dust (C_{dust}), and sorbed PFOA (C_{dPFOA})						
First exposure season (2007-2008)						
December '07	Personal	Personal	Personal	Personal	Personal	Personal
January '08	Personal	Personal	Personal	Personal	Platform	Platform
February '08	Personal	Personal	Personal	Personal	Personal	Platform
March '08	Personal	Personal	Personal	Personal	Personal	Platform
Second exposure season (2008-2009)						
December '08	Personal	Personal	Personal	Platform	Platform	Platform
January '09	Personal	Personal	Personal	Platform	Platform	Platform
February '09	Data from January '09					
March '09	personal	personal	Personal	Platform	Platform	Platform
Third exposure season (2009-2010)						
December '09 January '10 February '10 March '10	Platform (data from March '10)	Platform (data from March '10)	Personal (data from March '10)	Platform (data from March '10)	Personal (data from March '10)	Platform (data from March '10)
Fourth exposure season (2010-2011)						
December '10 January '11 February '11 March '11	Platform (data from March '10)	Platform (data from March '10)	Personal (data from March '10)	Platform (data from March '10)	Personal (data from March '10)	Platform (data from March '10)
Input data used for PFOA ($C_{airPFOA}$) and 8:2 FTOH ($C_{airFTOH}$) in air						
First exposure season						
December '07	Personal	Personal	Personal	Personal	Personal	Personal

January ‘08	Personal	Personal	Personal	Average	Average	Average
February ‘08	Personal	Personal	Personal	Average	Personal	Average
March ‘08	Personal	Platform	Personal	Platform	Personal	Platform
Second exposure season						
December ‘08	Personal	Personal	Personal	Platform	Platform	Platform
January ‘09	Personal	Platform	Platform	Platform	Platform	Platform
February ‘09	Data from January ‘09					
March ‘09	personal	Platform	Platform	Platform	Platform	Platform
Third exposure season (2009-2010)						
December ‘09 January ‘10 February ‘10 March ‘10	Platform (data from March ’10)	Platform (data from March ’10)	Personal (data from March ’10)	Platform (data from March ’10)	Personal (data from March ’10)	Platform (data from March ’10)
Fourth exposure season (2010-2011)						
December ‘10 January ‘11 February ‘11 March ‘11	Platform (data from March ’10)	Platform (data from March ’10)	Personal (data from March ’10)	Platform (data from March ’10)	Personal (data from March ’10)	Platform (data from March ’10)

Appendix 4. Variability of PFOA and 8:2 FTOH concentration in the cabin air

As shown in Figure A4-1, there were inter- and intra- individual variability in the personal measurements throughout the 2-year study. The PFOA and 8:2 FTOH concentrations measured by the personal pumps varied by up to two orders of magnitude from one technician to the other, during the same working day. For technicians that are affected by the ongoing exposure (i.e. technicians with low internal concentrations), it is therefore important to use the individual personal pump measurements as inputs. Furthermore, they varied over time and differences of up to one order of magnitude could be measured between successive months. Nevertheless, for a given month, the differences between platform pump and personal pump measurements were relatively small.

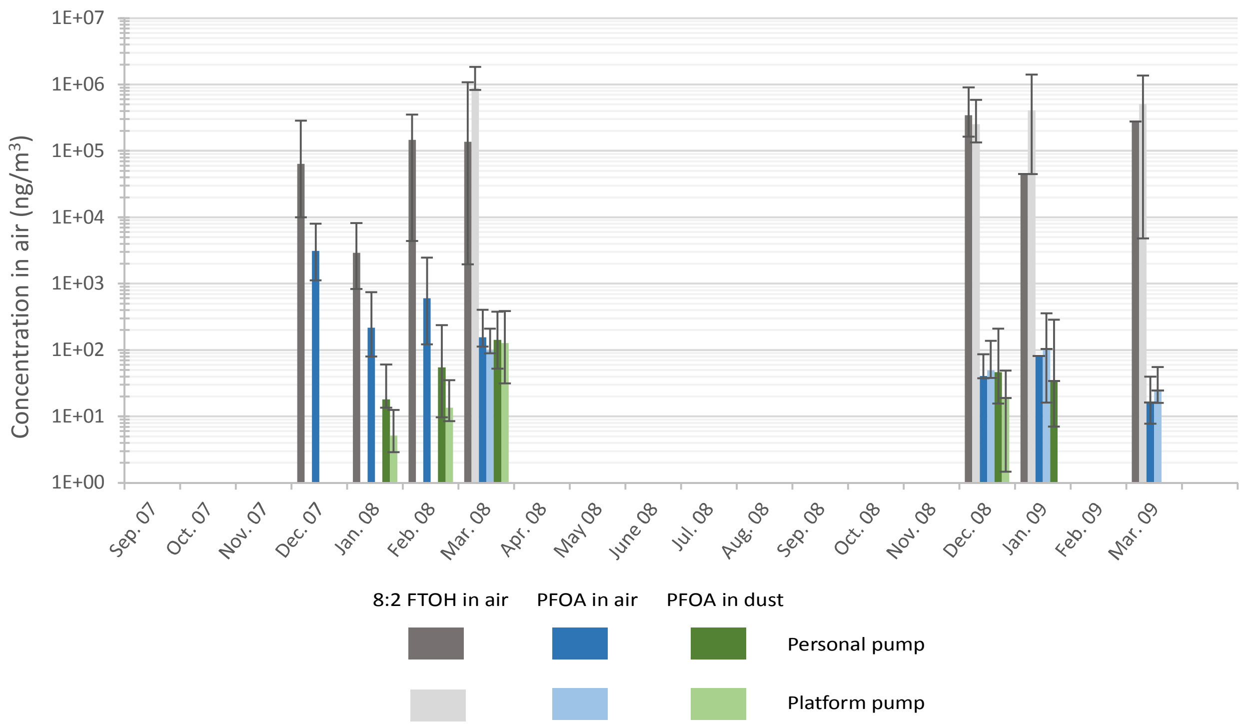


Figure A4-1: *Averaged concentrations of PFOA in air and dust, and 8:2 FTOH in air in the cabin environment. The measurements were obtained from platform pumps placed in the cabin (lighter-colored bars) and from personal pumps (darker-colored bars) placed on the technicians. The maximum and minimum values are represented by the error bars. No sampling was undertaken during February 2009. Platform pumps were first used from March 2008 and onwards for air measurements and from January 2008 and onwards for suspended dust. During* *the second exposure period, PFOA sorbed to suspended dust could not be detected in samples taken from the platform pumps (January 2009 and March 2009) and personal pumps (March 2009) reflecting probably the efficiency of the ventilated system to mitigate the particle levels in air.*

The following parameters can influence the amount of substance that is released daily in the cabin environment and that is further inhaled by the technician (they were not reported by Nilsson et al.[1,2]): 1) the type of activity (i.e. testing the skis on the snow, testing new wax combinations for a better slide performance, intensive waxing of multiple pairs of skis, etc.); 2) the kind of wax applied (e.g. kick waxes or glide waxes); 3) the protective safety equipment such as gloves and masks used in the cabin; and 4) behavior leading to atypically high exposures (i.e. eating, drinking in the cabin).

It was reported that a coffee machine was present in the cabin and eating and drinking could occur during work. As a consequence, hand-to-mouth contamination via food consumption and adsorption of PFOA from air to surface bottles and glasses could contribute to higher PFOA intake. Furthermore, the use of protective equipment during waxing such as gloves and masks was not common prior to the study as technicians had no awareness of chemical exposure. Shortly after the study started and the first results were communicated, precautions to mitigate exposure were initiated by the technicians with high internal concentration. Ventilation was installed in the cabin during the second year of the study.

Appendix 5. Additional model run for technician 8

An initial concentration for September 2007 was available for Technician 8. When accounting for this additional data during the simulation, the "goodness-of-fit" of the model was drastically reduced (R^2 = 0.35). Between September 2007 and December 2007, an increase of 60 ng/ml of PFOA in serum occurred. The exposure during these three months is unknown. Such an increase of PFOA in serum can only be explained by an exposure order of magnitudes higher than the exposure measured during the first ski wax season, or a sampling or analytical error. Modeling this time section was not possible and it was therefore decided to focus on the depurating phase starting in December 2007 to estimate $t_{1/2}$.

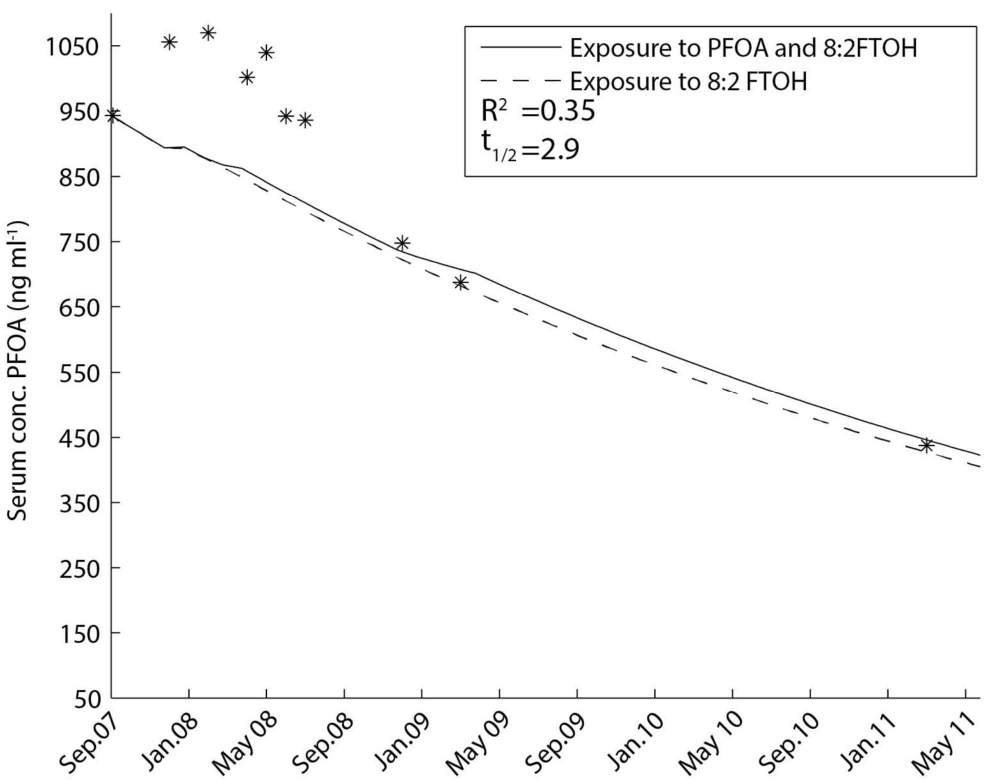


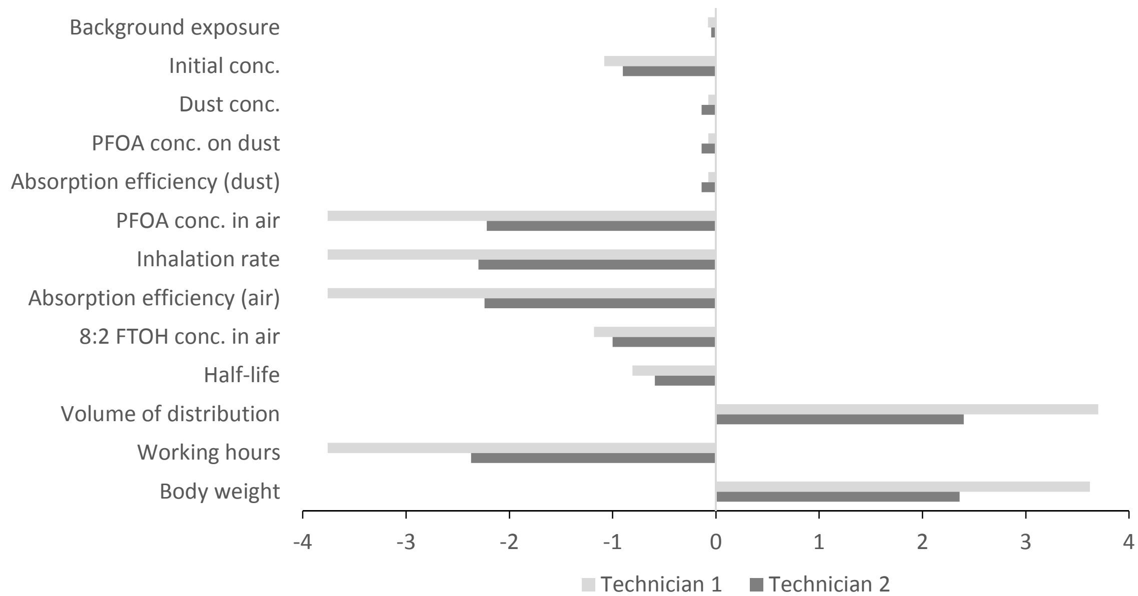
Figure A5-1: *Model results for technician 8, including the biomonitoring data from September 2007.*

Appendix 6. Sensitivity and uncertainty analysis

6.1 Sensitivity ratios

The calculation of the sensitivity ratio ($\frac{\Delta Output}{\Delta Input}$) is presented in the method section (2.3.3) of the main manuscript. The ratios are shown in Figure A6-1 for each technician. The sensitivity of a given input parameter *x* increases as $\mathrm{SR}_{\mathrm{y}}^{\mathrm{x}}$ approaches -1 or 1. A negative $\mathrm{SR}_{\mathrm{y}}^{\mathrm{x}}$ indicates that the effect on the output parameter *y* is inversely proportional to the change in the input parameter x (i.e. *y* decreases when *x* is increased), while a positive $\mathrm{SR}_{\mathrm{y}}^{\mathrm{x}}$ corresponds to a similar change for *x* and *y*.

a)



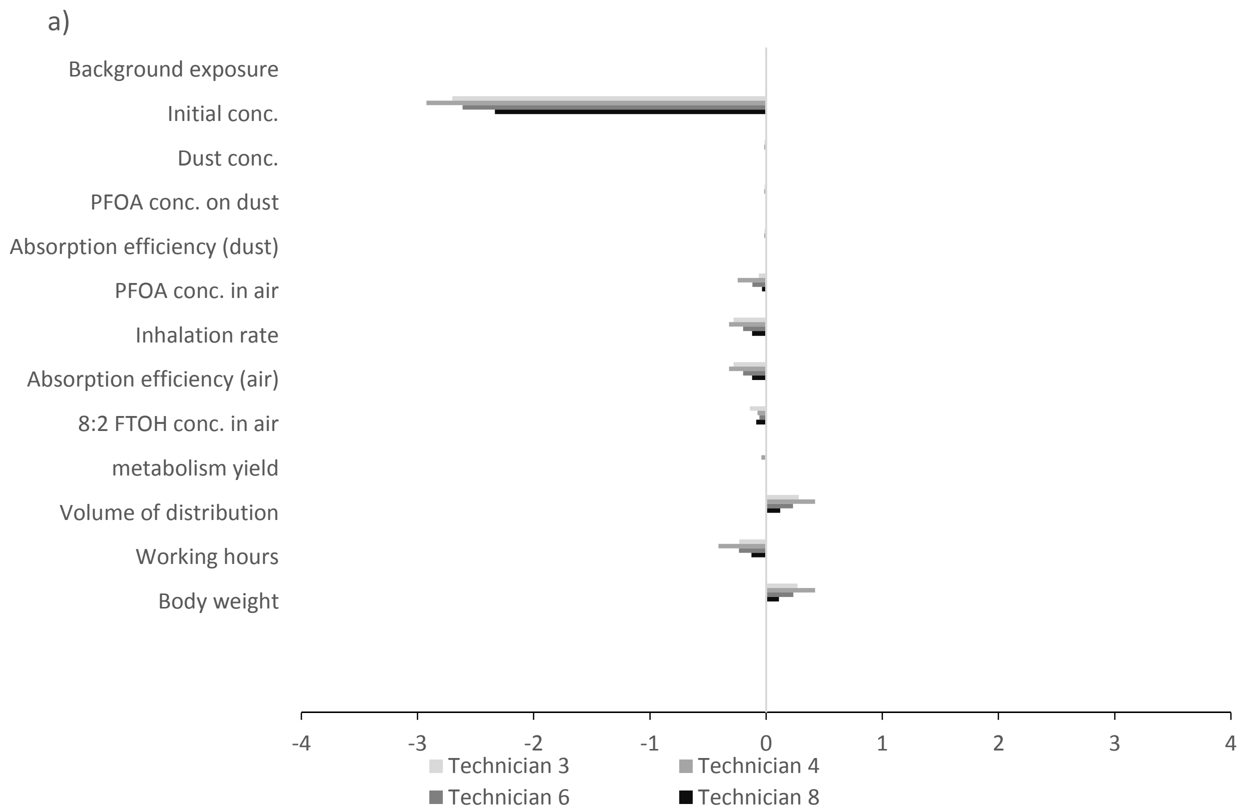


Figure A6-1. *Sensitivity ratios for the fitted output metabolism yield (Y_{meta}) (a) and elimination half-life ($t_{1/2}$) (b).*

6.2 Uncertainty analysis: assigned confidence factor

The uncertainty analysis couples the sensitivity ratio of each input parameter with their respective uncertainty (e.g. the confidence factor) in order to; 1) identify which input parameter is contributing the most to the overall uncertainty in the fitted Y_{meta} and $t_{1/2}$ and 2) estimate the margin of error of the fitted Y_{meta} and $t_{1/2}$. We applied the method of MacLeod et al.[3] to evaluate the uncertainty propagation from the input parameters to the fitted output parameters (metabolism yield (Y_{meta}) and elimination half-life ($t_{1/2}$)). A confidence factor was accordingly estimated for each input parameter (see section 2.3.3 as well as Eq. 7 and Eq. 8 in the main manuscript). The confidence factors were assigned based on the current knowledge available for each input parameter and on our best judgement. They are presented in Table A6-1, together with the arguments for their estimated values. These confidence factors were further used in Eq. 7 and Eq. 8 of the main manuscript to; 1) evaluate the contributions of the input parameters to the variance of each estimated Y_{meta} and $t_{1/2}$ and 2) estimate the confidence intervals (i.e. margins of error) for each estimated Y_{meta} and $t_{1/2}$.

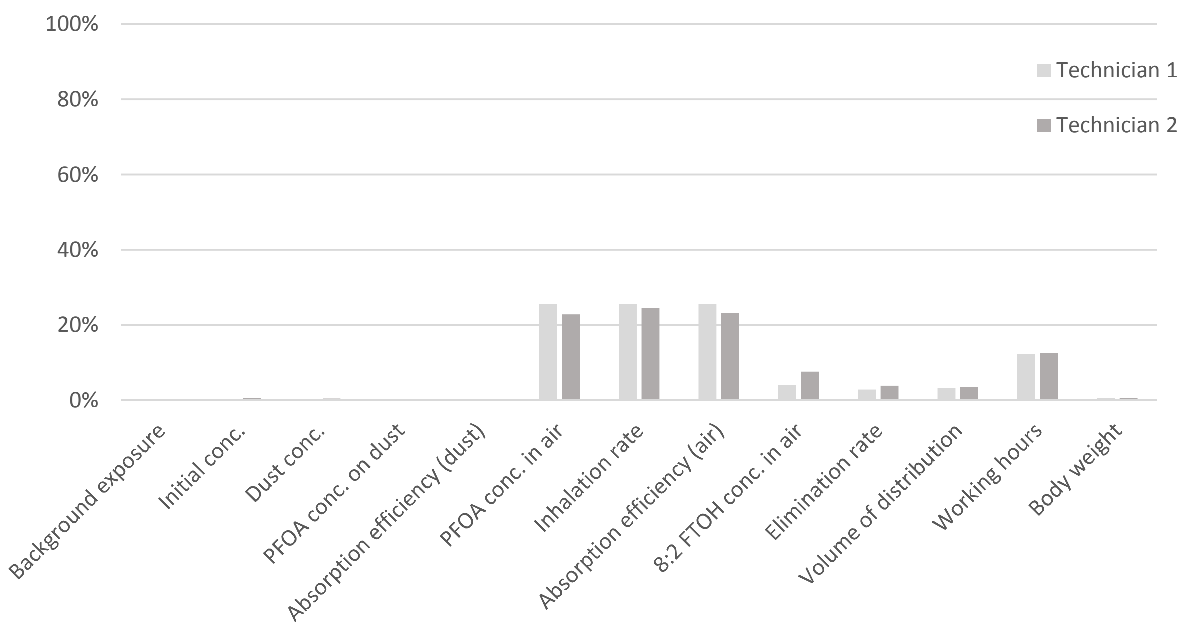
Table A6-1: *Assigned confidence factors for each input parameter in the PK model.*

Input parameter used in the model (I)	**Abbreviation**	**Arguments to estimate the confidence factor of each input parameter**	**Assigned confidence factor (Cf_I)**
Average daily intake of PFOA in the general population	C_{bkg}	The daily intake in Scandinavian population was estimated to be between 0.2 and 0.7 ng/kg/day.[4–6] The 5th and 95th percentile were assumed to be these values, respectively.	1.8
Concentration of 8:2 FTOH in air	$C_{airFTOH}$	Since the uncertainty may arise from the extrapolation of a monthly measurement to represent the weekly exposure, the intra-month variability was investigated for the estimation of Cf_I. The variability within a month was estimated based on the personal pump measurements of all technicians. Cf_I was estimated for each month and averaged.	1.4
Concentration of PFOA in air	$C_{airPFOA}$		1.5
Concentration of suspended dust particles in the cabin	C_{dust}		1.8
Concentration of PFOA sorbed to suspended dust	C_{dPFOA}		1.5

Initial concentration of PFOA in serum	C_{serum} *at t=0*	The uncertainty in the measurement of the initial serum concentrations is mainly caused by analytical imprecision. The confidence factor was estimated based on the initial concentration of technician 8, which was unusually low compared to the serum concentration measured in December 2007.	1.1
Absorption efficiency of PFOA/8:2 FTOH through the respiratory epithelium	E_i	As mentioned in Appendix 4, there are no experimental data on the absorption efficiency of PFOA through the lungs. In this study, we used a maximal value of 100% absorption. However, different assumptions and model scenarios were found in previous exposure studies, with a minimum of 50%[7] to a maximum of 100% absorption.[8,9]	1.3
Absorption efficiency of PFOA sorbed to suspended dust through the gastro-intestinal epithelium	E_{gi}	66 and 91% of gastro-intestinal absorption were considered as the 5th and 95th percentiles (see ref. 25)	1.1
Air inhalation rate [m^3/hour]	K_i	The US EPA[10] measured the inhalation rate of adults under different activity conditions (i.e. passive, light, moderate, high intensity). In our model, K_i was set as 0.67 m^3/hour (see Appendix 4 of the present document) which corresponds to the median value measured by US EPA for inhalation rate under light intensity physical activities. According to the same US EPA document, the 5^{th} and 95^{th} percentiles correspond to 0.54 and 0.87 m^3/hour, respectively.	1.3
Volume of distribution of PFOA	*Vd*	The interspecies variability observed in the volume of distribution of PFOA is rather low.[11–13] The 5^{th} and 95^{th} percentile was assumed to be 180 and 220 ml/kg, respectively.	1.1
hours of exposure per week	W_h	The variability of working hours per week over the length of the study was assumed to be moderate.	1.2
Body weight	B_w	The variability of body weight over the length of the study was assumed to be small.	1.04
Additional input parameter for fitting the metabolism yield			
Averaged elimination half-life	$t_{1/2}$	The elimination half-life used in the model for the fitting of the metabolism yield is the averaged intrinsic half-life estimated by Russell et al.[14] In their work, 2.1 and 2.7 were the 95% confidence interval. The confidence factor is therefore based on these two values.	1.1
Additional input parameter for fitting the half-life			
Averaged metabolism yield	Y_{meta}	The error range calculated for Ymeta in this section was used as the 5% and 95% confidence interval and Cf_I was defined accordingly (see Table A6-2 in Annex 6)	5.08

6.3 Uncertainty analysis: contribution of input uncertainty to the overall output uncertainty and margin of error of the estimated metabolism yield and elimination half-life

a)



b)

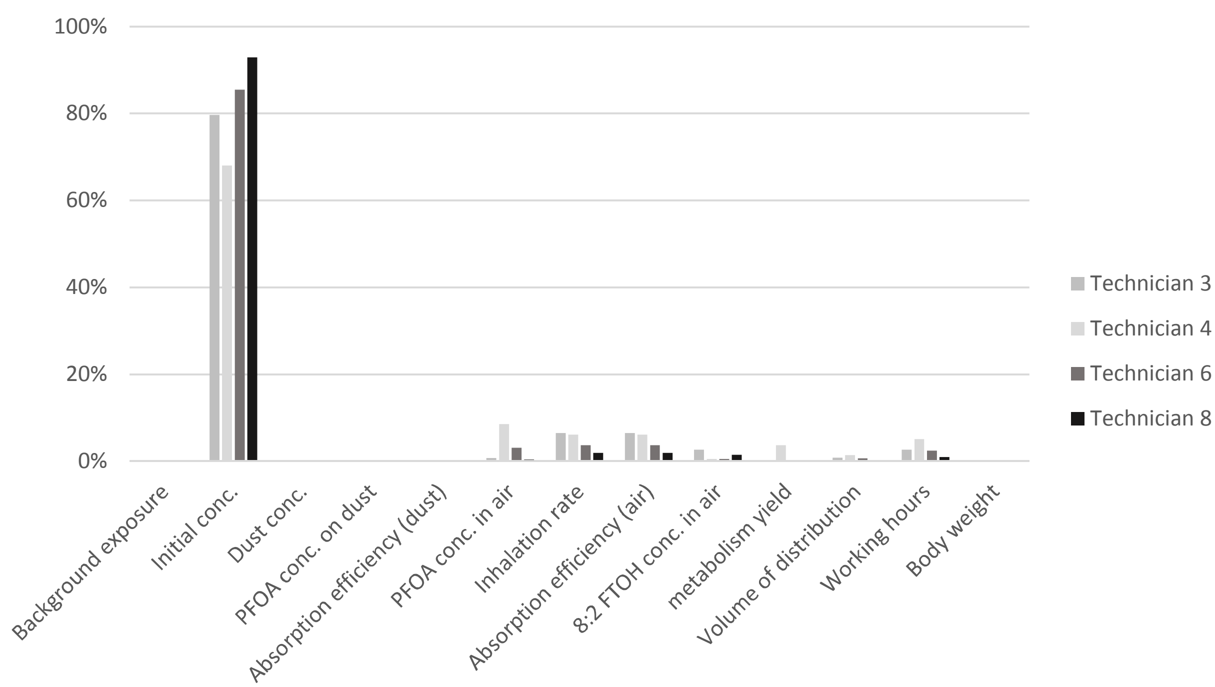


Figure A6-2. *Percentage contribution of uncertainty of individual input parameter to the overall uncertainty in fitting the metabolism yield (Y_{meta}) (a) and elimination half-life ($t_{1/2}$) (b).*

Table A6-2: *Confidence factors (Cf_o) and margin of error (5^{th} - 95^{th} percentile) for the estimated metabolism yield of each technician with low initial concentrations and for the estimated elimination half-life of each technician with high initial concentrations. The underlined values are based on molar concentrations.*

	Metabolism yield (<u>molar concentration basis</u>)		**Elimination half-life (years)**			
Technician	# 1	# 2	# 3	# 4	# 6	# 8
Estimated value	0.0027 <u>0.0030</u>	0.0026 <u>0.0029</u>	2.6	2.0	2.8	2.1
Confidence factor (Cf_o)	7.05	3.38	1.3	1.4	1.3	1.2
Margin of error (5^{th} - 95^{th} percentile)	0.0004-0.02 <u>0.0004-0.02</u>	0.0008-0.009 <u>0.0009-0.01</u>	1.8-3.6	1.5-2.6	2.1-3.6	1.8-2.6
Averaged Cf_o	5.2		1.3			
Margin of error (5^{th} - 95^{th} percentile) for the average output parameter, calculated from the averaged Cf_o	0.0005-0.01 <u>0.0006-0.01</u>		1.8-3.1			

Appendix 7. References

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