Calibrated (or otherwise fixed) values

Table 2
Values of the species-specific parameters after model calibration for the mouse, rat, monkey and human.

Parameters	Symbol	Mouse	Rat	Monkey	Human
Body weight, (Kg)[a]	BW	0.025	0.3	3.5	82.3
Cardia output, (L/h/kg$^{0.75}$)[b]	QCC	16.5	14	18.96	12.5
Fractional blood flows (% QC)[b]					
Liver	QLC	0.161	0.183	0.194	0.250
Kidney	QKC	0.091	0.141	0.123	0.175
Fractional volumes (% BW)[b]					
Liver	VLC	0.055	0.035	0.026	0.026
Kidney	VKC	0.017	0.0084	0.004	0.004
Plasma	VPlasC	0.049	0.0312	0.0448	0.0428
Filtrate[c]	VfilC	0.0017	0.00084	0.0004	0.0004
Volume of PTCs, (L/g kidney)[c]	VPTCC	1.35e-4	1.35e-4	1.35e-4	1.35e-4
Amount of proteins in PTCs[d] (mg/cell)	Protein	2.0e-6	2.0e-6	2.0e-6	2.0e-6
Hematocrit[e]	Htc	0.48	0.46	0.42	0.44
Partition coefficients[f]					
Liver	PL	7.65*	3.66*	3.72	2.03*
Kidney	PK	0.8	0.8	0.8	1.26
Rest	PRest	0.23*	0.26*	0.15*	0.2
Free fraction of PFOS in plasma[g]	Free	0.02*	0.09	0.016*	0.014*
Glomerular filtration rate constant, (L/h/kg of kidney)[h]	GFRC	59	62.1	21.85	24.19
Gastric emptying rate constant, (/h/kg BW$^{0.25}$)[i]	GEC	0.54	0.54	2.34	3.51
Transporter rates[j]					
Vmax of basolateral (pmol/mg protein/min)	Vmax_baso_invitro	393.45	393.45	439.2	479*
Km of basolateral (mg/L)	Km_baso	27.2	27.2	20.1	20.1
Vmax of apical (pmol/mg protein/min)	Vmax_apical_invitro	4185*	1808*	76972*	51803*
Km of apical transporters (mg/L)	Km_api	52.3	278*	45.2*	64.4*
Relative activity factor[j]					
Apical transporters (unitless)	RAF_api	2.81*	1.90*	0.0014*	0.001*
Basolateral transporters (unitless)	RAF_baso	3.99	4.15*	1	1
Other rate constants (/h/kg BW$^{0.25}$)[j]					
Uptake from stomach to liver,	K0C	1	1	1	1
Absorption from small intestines to liver	KabsC	1.10*	2.12	2.12	2.12
Unabsorbed dose to appear in feces	KunabsC	7.05e-5	7.05e-5	7.05e-5	7.05e-5
Rate of efflux of PFOS from PTCs into blood	KeffluxC	5.60*	2.09*	0.1	0.15*
Diffusion rate from PTCs	Kdif	4.6e-5*	5.1e-4*	0.001	0.001
Biliary elimination rate	KbileC	3.9e-4*	0.0026*	7.8e-4*	1.3e-4*
Urinary elimination rate	KurineC	1.60	1.60	0.092*	0.096*

* Calibrated values were fitted (the initiate values are provided in Table S1) with experiment data using the Levenberg-Marquardt algorithm.
[a] Use measured value if available, or collected from Brown et al. (1997) for rodents and monkeys and from ICRP (2002) for humans.
[b] The baseline value was obtained from Brown et al. (1997).
[c] The baseline value was assumed to be 10% kidney volume based on Worley and Fisher (2015) and Worley et al. (2017b).
[d] The baseline value was obtained from Addis et al. (1936) and Hsu et al. (2014).
[e] The baseline value was obtained from Hejtmancik et al. (2002) (mouse); Davies and Morris (1993) (Rat); Choi et al. (2016) (Monkey); ICRP (2002) (human).
[f] Loccisano et al. (2012) (mouse and rat) and Loccisano et al. (2011) (monkey); Fabrega et al. (2014) (human).
[g] The baseline values were obtained from Loccisano et al. (2012) (mouse and rat) and Loccisano et al. (2011) (monkey and human).
[h] Qi et al. (2004) (mouse), Corley et al. (2005) (rat and human), Iwama et al. (2014) (monkey).
[i] Yang et al. (2015) (mouse, rat and human), Fisher et al. (2011) (monkey).
[j] Initiate values were assumed to be equal to those of PFOA adopted from Worley and Fisher (2015) (rat and mouse) and Worley et al. (2017b) (human and monkey), and then were re-estimated in the present model.

After calibration comes posterior sampling

- Given the models, the fixed parameters and observed data we can evaluate the value of the posterior at any parameter value

$$p(\theta, \mu, \Sigma^2, \sigma^2 \mid y, \phi, E, t) \propto p(y \mid \theta, \sigma^2, \phi, E, t) p(\theta \mid \mu, \Sigma^2) p(\mu) p(\Sigma^2) p(\sigma^2)$$

- We draw a sample from it using Markov Chain Monte Carlo methods
  - We can also investigate whether or not MCMC sampler worked ok (“converged”)
  - Given a set of samples from a posterior, we can calculate the sample mean of any function of $(\theta, \mu, \Sigma^2, \sigma^2)$
    - Including its uncertainty!