Predicting human equivalent dose

Compared species : rats and monkeys

- Find the posterior distribution of parameters and validate models via model prediction
- Use the validated models to predict response (plasma & liver) under no-observed-adverse-effect-level (NOAEL) doses of PFOS
  - rats : 0.34 mg/kg/day
  - monkeys : 0.15 mg/kg/day
- Calculate (plasma & liver) AUC at NOEAL exposure levels
  - rats [14 weeks] & humans [25 years]
  - monkeys [26 weeks] & humans [25 years]

$$\mathrm{HED} = \frac{\mathrm{AUC}_{\mathrm{species}}/\mathrm{duration}_{\mathrm{species}}}{\mathrm{AUC}_{\mathrm{human}}/\mathrm{duration}_{\mathrm{human}}} \cdot \mathrm{NOAEL}_{\mathrm{species}}$$

HED of the study

Table 4
Human equivalent doses (HED) derived from the rat and monkey models based on the model-predicted average serum concentrations in each species.

Study; species; critical effects	Dosing duration (days)	NOAEL (mg/kg/day)	ASC[a] or ALC[b] at NOAEL (μg/mL or mg/L)		HED (mg/kg/day)	
			EPA	This study	EPA[d]	This study[e]
Seacat et al., 2002: Monkey; (Increased liver weight; histopathology change; Decreased body weight)	182	0.15	38	ASC: 0.56 (95% CI: 0.015–1.30)[c] ALC: 182 (95% CI: 80–288)	0.0031	Plasma: 0.0055 (95% CI: 0.0001–0.14) Liver: 0.012 (95% CI: 0.004–0.22)
Seacat et al., 2003: Rat; (Increased liver weight; centrilobular hepatocytic vacuolation)	98	0.34	16.5	ASC: 0.46 (95% CI: 0.034–2.77)[c] ALC: 56 (95% CI: 33–125)	0.0013	Plasma: 0.0057 (95% CI: 0.0002–0.17) Liver: 0.004 (0.0013–0.072)

[a] ASC represents the average serum concentration at the NOAEL exposure level for each species. ASC (mg/L) = Serum-AUC (mg/L * h) ÷ (24 h/day × Exposure duration [Days]).
[b] ALC represents the average liver concentration at the NOAEL exposure level for each species. ALC (mg/L) = Liver-AUC (mg/L * h) ÷ (24 h/day x Exposure duration [Days]).
[c] Mean (95% confidence interval).
[d] HED = average serum concentration (mg/L) × CL, where CL = 0.000081 (L/kg bw/day) (EPA, 2016b).
[e] HED = NOAEL × ($ASC_{\_aniaml}/ASC_{\_human}$) or ($ALC_{\_aniaml}/ALC_{\_human}$).