

Table S1. Models evaluated*Final model (#5) is shown in bold*

Linear models										
Model	Description	OBJ	Intercept (α)	Slope (β)	$\omega^2_{intercept}$ (η_α)	ω^2_{slope} (η_β)	Occ (η_α)	σ^2 (additive)	σ^2 (proportional)	
1	Intercept, no slope; IIV additive	8448	3.08 (33%)		57.5 (25%)			81.4 (8%)		
2	Intercept, no slope; IIV additive fixed	9100	3.02 (34%)		0 [fixed]			139 (12%)		
3	Intercept, slope; IIV additive (intercept only)	8216	-0.333 (375%)	0.0011 (14%)	60.3 (23%)			69.5 (8%)		
4	Intercept, slope; IIV additive (intercept & slope)	8088	-0.446 (280%)	0.0012 (15%)	78.3 (21%)	0		59.2 (7%)		
5	Intercept, slope; IIV additive (intercept); IOV additive; residual error additive	7738	-0.783 (139%)	0.0013 (8%)	36.6 (42%)		47.9 (20%)	45.5 (6%)		
6	Intercept, slope; IIV additive (intercept); IOV additive; residual error proportional	7877	12.2 (18%)	0.0008 (18%)	179 (40%)		46.2 (20%)		0.225 (36%)	
7	Intercept, slope; IIV additive (intercept); IOV additive; residual error additive + proportional	7737	-0.726 (145%)	0.0013 (8%)	36.7 (42%)		47.8 (20%)	44.7 (7%)	0.0331 (173%)	
8	Intercept, slope; IIV additive (intercept & slope); IOV additive intercept; residual error additive	7730	-0.754 (145%)	0.0013 (8%)	36.6 (43%)	0	47.7 (20%)	44.4 (7%)		
E_{max} models										
Model	Description	OBJ	E _{max}	EC ₅₀	Gamma	E ₀	ω^2_{EC50}	ω^2_{E0}	ω^2_{Emax}	σ^2 (additive)
9	E ₀ , EC ₅₀ , E _{max} , Gamma (fixed)	8185	20.3 (13%)	3120 (56%)	1 [fixed]	-3.19 (35%)	8 (34%)	1.13 (43%)	0.283 (47%)	62.1 (7%)
10	E ₀ , EC ₅₀ , E _{max} , Gamma (fixed)	8392	22.1 (11%)	2500 (56%)	1 [fixed]	-5.97 (78%)	7.02 (28%)			78.3 (8%)

Model fit to the data was evaluated on the following goodness-of-fit criteria: a minimum 3.84 point ($p < 0.05$) decrease in the value of the objective function according to the log-likelihood ratio test; increased precision of estimated parameters; decrease in IIV, and decrease in random residual variability.

Additional criteria were: good agreement between observed and predicted ddQTcF; uniformly scattered weighted residuals versus predicted ddQTcF; visual predictive check and bootstrap analysis.