

$$\begin{aligned} > la1 := - \frac{1 \cdot ((k01 + k21 + k12) - ((k01 + k21 + k12)^2 - 4 \cdot k01 \cdot k12)^{0.5})}{2} \\ la1 := - \frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5} \end{aligned} \quad (1)$$

$$\begin{aligned} > la2 := - \frac{1 \cdot ((k01 + k21 + k12) + ((k01 + k21 + k12)^2 - 4 \cdot k01 \cdot k12)^{0.5})}{2} \\ la2 := - \frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} k12 - \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5} \end{aligned} \quad (2)$$

$$\begin{aligned} > a := \frac{(k01 + k21 + la1)}{k12} \\ a := \frac{\frac{1}{2} k01 + \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}}{k12} \end{aligned} \quad (3)$$

$$\begin{aligned} > b := \frac{k21}{(k12 + la2)} \\ b := \frac{k21}{\frac{1}{2} k12 - \frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}} \end{aligned} \quad (4)$$

$$\begin{aligned} > x1s := \frac{\left( \frac{Dose}{\tau} \right)}{k01} \\ x1s := \frac{Dose}{\tau k01} \end{aligned} \quad (5)$$

$$\begin{aligned} > x2s := x1s \cdot \left( \frac{k21}{k12} \right) \\ x2s := \frac{Dose k21}{\tau k01 k12} \end{aligned} \quad (6)$$

$$\begin{aligned} > y1s := \frac{\rho}{k01} \\ y1s := \frac{\rho}{k01} \end{aligned} \quad (7)$$

$$\begin{aligned} > y2s := y1s \cdot \left( \frac{k21}{k12} \right) \\ y2s := \frac{\rho k21}{k01 k12} \end{aligned} \quad (8)$$

$$\begin{aligned} > M1 := \frac{((x10 - x1s) \cdot b - (x20 - x2s))}{(b - a)} \\ M1 := \left( \frac{\left( x10 - \frac{Dose}{\tau k01} \right) k21}{\frac{1}{2} k12 - \frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}} - x20 \right) \end{aligned} \quad (9)$$

$$\left. \left( \frac{Dose \cdot k_{21}}{\tau \cdot k_{01} \cdot k_{12}} \right) \right/$$

$$\left( \frac{\frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}}}}{\frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}}}{k_{12}}} \right)$$

$$> M2 := \frac{((x_{20} - x_{2s}) - (x_{10} - x_{1s}) \cdot a)}{(b - a)}$$

$$M2 := \left( x_{20} - \frac{Dose \cdot k_{21}}{\tau \cdot k_{01} \cdot k_{12}} \right. \tag{10}$$

$$- \frac{1}{k_{12}} \left( \left( x_{10} - \frac{Dose}{\tau \cdot k_{01}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5} \right) \right) \left. \right) \left/ \right.$$

$$\left( \frac{\frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}}}}{\frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}}}{k_{12}}} \right)$$

$$> x_{1tau} := M1 \cdot \exp(la1 \cdot \tau) + M2 \cdot \exp(la2 \cdot \tau) + x_{1s}$$

$$x_{1tau} := \left( \left( \frac{\left( x_{10} - \frac{Dose}{\tau \cdot k_{01}} \right) k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}} - x_{20} \right. \right.$$

$$\left. \left. + \frac{Dose \cdot k_{21}}{\tau \cdot k_{01} \cdot k_{12}} \right) e^{\left( -\frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5} \right) \tau} \right) \left/ \right.$$

$$\left( \frac{\frac{k21}{\frac{1}{2} k12 - \frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}}}{\frac{1}{2} k01 + \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}}}{k12} \right)$$

$$+ \left( \left( x20 - \frac{Dose k21}{\tau k01 k12} - \frac{\left( x10 - \frac{Dose}{\tau k01} \right) \left( \frac{1}{2} k01 + \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5} \right)}{k12} \right) \right)$$

$$\left( \frac{\frac{k21}{\frac{1}{2} k12 - \frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}}}{\frac{1}{2} k01 + \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}}}{k12} \right) + \frac{Dose}{\tau k01}$$

>  $x2tau := M1 \cdot a \cdot \exp(la1 \cdot \tau) + M2 \cdot b \cdot \exp(la2 \cdot \tau) + x2s$

$$x2tau := \left( \left( \frac{\left( x10 - \frac{Dose}{\tau k01} \right) k21}{\frac{1}{2} k12 - \frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}} - x20 + \frac{Dose k21}{\tau k01 k12} \right) \left( \frac{1}{2} k01 + \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5} \right) e^{\left( -\frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5} \right) \tau} \right) /$$

$$\left( \left( \frac{\frac{k21}{\frac{1}{2} k12 - \frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}}}{\frac{1}{2} k01 + \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}}}{k12} \right) k12 \right)$$

$$+ \left( \left( x_{20} - \frac{Dose \cdot k_{21}}{\tau \cdot k_{01} \cdot k_{12}} - \frac{\left( x_{10} - \frac{Dose}{\tau \cdot k_{01}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12}) \right)}{k_{12}} \right. \right.$$

$$\left. \left( \left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}} - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}}{k_{12}} \right) \left( \frac{1}{2} k_{12} \right. \right. \right.$$

$$\left. \left. - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5} \right) \right) + \frac{Dose \cdot k_{21}}{\tau \cdot k_{01} \cdot k_{12}}$$

$$> NI := \frac{\left( (x_{1\tau} - y_{1s}) \cdot b - \frac{(x_{2\tau} - y_{2s})}{1} \right)}{(b - a)}$$

$$NI := \left( \left( \left( \left( \frac{\left( x_{10} - \frac{Dose}{\tau \cdot k_{01}} \right) k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}} - x_{20} \right. \right. \right. \right.$$

$$\left. \left. \left. + \frac{Dose \cdot k_{21}}{\tau \cdot k_{01} \cdot k_{12}} \right) e^{\left( -\frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5} \right) \tau} \right) \right) /$$

$$\left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}} \right)$$

$$\left. - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}} \right)$$

$$+ \left( \left( x_{20} - \frac{Dose k_{21}}{\tau k_{01} k_{12}} - \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right)}{k_{12}} \right) \right)$$

$$\left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} \right)$$

$$\left. - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}} \right) + \frac{Dose}{\tau k_{01}}$$

$$\left. - \frac{\rho}{k_{01}} \right) k_{21} \left. \left( \frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right) \right)$$

$$-4 k_{01} k_{12})^{0.5})$$

$$- \left( \left( \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} - x_{20} + \frac{Dose k_{21}}{\tau k_{01} k_{12}}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right) \right)$$

$$-4 k_{01} k_{12})^{0.5}) e^{\left( -\frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right) \tau} \Bigg) /$$

$$\left( \left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} \right) \right)$$

$$- \left. \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}}} \right) k_{12} \Bigg)$$

$$- \left( \left( x_{20} - \frac{Dose k_{21}}{\tau k_{01} k_{12}} - \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right)}{k_{12}}} \right) \right)$$

$$\left( \left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}} - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}}{k_{12}}} \right) \left( \frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5} \right) - \frac{Dose k_{21}}{\tau k_{01} k_{12}} \right)$$

$$\left. + \frac{\rho k_{21}}{k_{01} k_{12}} \right)$$

$$\left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}} - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}}{k_{12}}} \right)$$

$$> N2 := \frac{\left( (x_{2\tau} - y_{2s}) - \frac{(x_{1\tau} - y_{1s}) \cdot a}{1} \right)}{(b - a)}$$

$$\begin{aligned}
 N2 := & \left( \left( \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} - x_{20} \right. \right. \\
 & \left. \left. + \frac{Dose k_{21}}{\tau k_{01} k_{12}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 \right. \right. \right. \\
 & \left. \left. \left. - 4 k_{01} k_{12} \right)^{0.5} \right) e^{\left( -\frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right) \tau} \right) /
 \end{aligned}$$



$$\left( \left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}} \right. \right.$$

$$\left. \left. - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}}{k_{12}} \right) k_{12} \right)$$

$$+ \left( \left( x_{20} - \frac{Dose k_{21}}{\tau k_{01} k_{12}} - \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5} \right)}{k_{12}} \right. \right.$$

$$\left. \left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}} \right. \right.$$

$$- \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}} \left( \frac{1}{2} k_{12} \right)$$

$$- \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \left( \frac{Dose k_{21}}{\tau k_{01} k_{12}} \right)$$

$$- \frac{\rho k_{21}}{k_{01} k_{12}}$$

$$- \frac{1}{k_{12}} \left( \left( \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} \right) \right)$$

$$- x_{20} + \frac{Dose k_{21}}{\tau k_{01} k_{12}} \left( e^{\left( -\frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right) \tau} \right) /$$

$$\left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}} - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}}{k_{12}} \right)$$

$$+ \left( \left( x_{20} - \frac{Dose k_{21}}{\tau k_{01} k_{12}} - \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5} \right)}{k_{12}} \right) \right)$$

$$\left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}} - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5}}{k_{12}} \right) + \frac{Dose}{\tau k_{01}}$$

$$- \frac{\rho}{k_{01}} \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} ((k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12})^{0.5} \right)$$

$$\left( \frac{\frac{k21}{\frac{1}{2} k12 - \frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}}}{\frac{1}{2} k01 + \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}}}{k12} \right)$$

> eq1 := NI = 190.862

$$eq1 := \left( \left( \left( \left( \frac{\left( x10 - \frac{Dose}{\tau k01} \right) k21}{\frac{1}{2} k12 - \frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}} - x20}{\frac{1}{2} k01 + \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}} \right) \right) \right) e^{\left( -\frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5} \right) \tau} + \frac{Dose k21}{\tau k01 k12} \right) /$$

$$\left( \frac{\frac{k21}{\frac{1}{2} k12 - \frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}}}{\frac{1}{2} k01 + \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5}}}{k12} \right)$$

$$+ \left( \left( x_{20} - \frac{Dose \cdot k_{21}}{\tau \cdot k_{01} \cdot k_{12}} - \frac{\left( x_{10} - \frac{Dose}{\tau \cdot k_{01}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right) \right)}{k_{12}} \right. \right.$$

$$\left. \left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} \right. \right.$$

$$\left. - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}} \right) + \frac{Dose}{\tau \cdot k_{01}}$$

$$\left. - \frac{\rho}{k_{01}} \right) k_{21} \left. \left( \frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 \right. \right. \right.$$

$$\left. - 4 k_{01} k_{12} \right)^{0.5} \left. \right)$$

$$- \left( \left( \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} - x_{20} + \frac{Dose k_{21}}{\tau k_{01} k_{12}}} \right) \left( \frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right) e^{\left( -\frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right) \tau} \right) /$$

$$\left( \left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}}} \right) k_{12} \right)$$

$$- \left( \left( x_{20} - \frac{Dose k_{21}}{\tau k_{01} k_{12}} - \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right)}{k_{12}} \right) \right)$$

$$\left( \left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}}} \right) \left( \frac{1}{2} k_{12} \right) \right)$$

$$\left. -\frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right) - \frac{Dose k_{21}}{\tau k_{01} k_{12}}$$

$$\left. + \frac{\rho k_{21}}{k_{01} k_{12}} \right)$$

$$\left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}} \right) = 190.862$$

> eq2 := N2 = 195.523

$$eq2 := \left( \left( \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} - x_{20} \right) \right)$$

$$+ \frac{Dose \ k21}{\tau \ k01 \ k12} \left( \frac{1}{2} k01 + \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2$$

$$- 4 \ k01 \ k12)^{0.5} \right) e^{\left( -\frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 \ k01 \ k12)^{0.5} \right) \tau} \Bigg) /$$

$$\left( \left( \frac{k21}{\frac{1}{2} k12 - \frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} ((k01 + k21 + k12)^2 - 4 \ k01 \ k12)^{0.5}} \right) \right)$$



$$- \left. \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}} \right\} k_{12}$$

$$+ \left( \left( x_{20} - \frac{Dose k_{21}}{\tau k_{01} k_{12}} - \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right)}{k_{12}} \right) \right.$$

$$\left. \left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} \right) \right.$$

$$\left. - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}} \right) \left( \frac{1}{2} k_{12} \right)$$

$$-\frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \left) + \frac{Dose k_{21}}{\tau k_{01} k_{12}}$$

$$-\frac{\rho k_{21}}{k_{01} k_{12}}$$

$$-\frac{1}{k_{12}} \left( \left( \left( \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} \right)} \right) \right)$$

$$-x_{20} + \frac{Dose k_{21}}{\tau k_{01} k_{12}} \left) e^{\left( -\frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right) \tau} \right) /$$

$$\left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} \right)$$

$$\begin{aligned}
& - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}} \Bigg) \\
& + \left( \left( x_{20} - \frac{Dose k_{21}}{\tau k_{01} k_{12}} - \frac{\left( x_{10} - \frac{Dose}{\tau k_{01}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right)}{k_{12}} \right. \right. \\
& \left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} \right. \\
& \left. \left. - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}} \right) + \frac{Dose}{\tau k_{01}} \right. \\
& \left. \left. - \frac{\rho}{k_{01}} \right) \left( \frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5} \right) \right) \Bigg)
\end{aligned}$$

$$\left( \frac{k_{21}}{\frac{1}{2} k_{12} - \frac{1}{2} k_{01} - \frac{1}{2} k_{21} - \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}} - \frac{\frac{1}{2} k_{01} + \frac{1}{2} k_{21} - \frac{1}{2} k_{12} + \frac{1}{2} \left( (k_{01} + k_{21} + k_{12})^2 - 4 k_{01} k_{12} \right)^{0.5}}{k_{12}} \right) = 195.523$$

> eq3 := la1 = -6.298 · 10<sup>-3</sup>

$$eq3 := -\frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} k12 + \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5} = -0.006298000000 \quad (17)$$

$$> eq4 := la2 = -0.052$$

$$eq4 := -\frac{1}{2} k01 - \frac{1}{2} k21 - \frac{1}{2} k12 - \frac{1}{2} ((k01 + k21 + k12)^2 - 4 k01 k12)^{0.5} = -0.052 \quad (18)$$

$$> Dose := 2500; \tau := 1; \rho := 0; x10 := 0; x20 := 0$$

$$Dose := 2500$$

$$\tau := 1$$

$$\rho := 0$$

$$x10 := 0$$

$$x20 := 0 \quad (19)$$

$$> solve([eq1, eq2, eq3, eq4], [k01, k21, k12])$$

[ ]

(20)

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