# <u>Useful Pharmacokinetic Equations</u>

## Symbols

D = dose
$\tau$ = dosing interval
CL = clearance
Vd = volume of distribution
$k_e$ = elimination rate constant
$k_a$ = absorption rate constant
F = fraction absorbed (bioavailability)
$K_0$ = infusion rate
T = duration of infusion
C = plasma concentration

## General

**Elimination rate constant**

$$k_e = \frac{CL}{Vd} = \frac{\ln\left(\frac{C_1}{C_2}\right)}{(t_2 - t_1)} = \frac{\ln C_1 - \ln C_2}{(t_2 - t_1)}$$

**Half-life**

$$t_{1/2} = \frac{0.693 \cdot Vd}{CL} = \frac{\ln(2)}{k_e} = \frac{0.693}{k_e}$$

## Intravenous bolus

**Initial concentration**

$$C_0 = \frac{D}{Vd}$$

**Plasma concentration (single dose)**

$$C = C_0 \cdot e^{-k_e \cdot t}$$

**Plasma concentration (multiple dose)**

$$C = \frac{C_0 \cdot e^{-k_e \cdot t}}{\left(1 - e^{-k_e \cdot \tau}\right)}$$

**Peak (multiple dose)**

$$C_{max} = \frac{C_0}{\left(1 - e^{-k_e \cdot \tau}\right)}$$

**Trough (multiple dose)**

$$C_{min} = \frac{C_0 \cdot e^{-k_e \cdot \tau}}{\left(1 - e^{-k_e \cdot \tau}\right)}$$

**Average concentration (steady state)**

$$\overline{C}p_{ss} = \frac{D}{CL \cdot \tau}$$

## Oral administration

**Plasma concentration (single dose)**

$$C = \frac{F \cdot D \cdot k_a}{Vd(k_a - k_e)} \cdot \left(e^{-k_e \cdot t} - e^{-k_a \cdot t}\right)$$

**Time of maximum concentration (single dose)**

$$t_{max} = \frac{\ln\left(\frac{k_a}{k_e}\right)}{(k_a - k_e)}$$

**Plasma concentration (multiple dose)**

$$C = \frac{F \cdot D \cdot k_a}{Vd(k_a - k_e)} \cdot \left(\frac{e^{-k_e \cdot t}}{\left(1 - e^{-k_e \cdot \tau}\right)} - \frac{e^{-k_a \cdot t}}{\left(1 - e^{-k_a \cdot \tau}\right)}\right)$$

**Time of maximum concentration (multiple dose)**

$$t_{max} = \frac{\ln\left(\frac{k_a \cdot \left(1 - e^{-k_e \cdot \tau}\right)}{k_e \cdot \left(1 - e^{-k_a \cdot \tau}\right)}\right)}{(k_a - k_e)}$$

**Average concentration (steady state)**

$$\overline{C} = \frac{F \cdot D}{CL \cdot \tau}$$

**Clearance**

$$Cl = \frac{Dose \cdot F}{AUC}$$

$$Cl = k_e \cdot V_d$$

# Constant rate infusion

### Plasma concentration (during infusion)

$$C = \frac{k_0}{CL} \cdot \left(1 - e^{-k_e \cdot t}\right)$$

### Plasma concentration (steady state)

$$C = \frac{k_0}{CL}$$

### Calculated clearance (Chiou equation)

$$CL = \frac{2 \cdot k_0}{\left(C_1 + C_2\right)} + \frac{2 \cdot Vd \cdot \left(C_1 - C_2\right)}{\left(C_1 + C_2\right) \cdot \left(t_2 - t_1\right)}$$

# Short-term infusion

### Peak (single dose)

$$C_{max(1)} = \frac{D}{CL \cdot T} \cdot \left(1 - e^{-k_e \cdot T}\right)$$

### Trough (single dose)

$$C_{min(1)} = C_{max(1)} \cdot e^{-k_e \cdot (\tau - T)}$$

### Peak (multiple dose)

$$C_{max} = \frac{D}{CL \cdot T} \cdot \frac{\left(1 - e^{-k_e \cdot T}\right)}{\left(1 - e^{-k_e \cdot \tau}\right)}$$

### Trough (multiple dose)

$$C_{min} = C_{max} \cdot e^{-k_e \cdot (\tau - T)}$$

### Calculated elimination rate constant

$$k_e = \frac{\ln\left(\frac{C^*_{max}}{C^*_{min}}\right)}{\Delta t}$$

with $C_{max}^*$ = measured peak and $C_{min}^*$ = measured trough,
measured over the time interval $\Delta t$

### Calculated peak

$$C_{max} = \frac{C^*_{max}}{e^{-k_e \cdot t^*}}$$

with $C_{max}^*$ = measured peak, measured at time $t^*$ after the end of the infusion

### Calculated trough

$$C_{min} = C^*_{min} \cdot e^{-k_e \cdot t^*}$$

with $C_{min}^*$ = measured trough, measured at time $t^*$ before the start of the next infusion

### Calculated volume of distribution

$$Vd = \frac{D}{k_e \cdot T} \cdot \frac{\left(1 - e^{-k_e \cdot T}\right)}{[C_{max} - (C_{min} \cdot e^{-k_e \cdot T})]}$$

### Calculated recommended dosing interval

$$\tau = \frac{\ln\left(\frac{C_{max(desired)}}{C_{min(desired)}}\right)}{k_e} + T$$

### Calculated recommended dose

$$D = C_{max(desired)} \cdot k_e \cdot V \cdot T \cdot \frac{\left(1 - e^{-k_e \cdot \tau}\right)}{\left(1 - e^{-k_e \cdot T}\right)}$$

# Two-Compartment-Body Model

$$C = a \bullet e^{-\alpha t} + b \bullet e^{-\beta t}$$

$$AUC_{\infty} = a / \alpha + b / \beta$$

$$Vd_{area} > Vd_{ss} > Vc$$

### Creatinine Clearance

$$CL_{creat}(male) = \frac{(140 - age) \bullet weight}{72 \bullet Cp_{creat}}$$

$$CL_{creat}(female) = \frac{(140 - age) \bullet weight}{85 \bullet Cp_{creat}}$$

With weight in kg, age in years, creatinine plasma conc. in mg/dl and $CL_{creat}$ in ml/min

## $K_e$ for aminoglycosides

$K_e = 0.00293(CrCL) + 0.014$

## Metabolic and Renal Clearance

$$E_H = \frac{Cl_{int} \cdot fu_b}{Q_H + Cl_{int} \cdot fu_b}$$

$$Cl_H = E_H \cdot Q_H = \frac{Q_H \cdot Cl_{int} \cdot fu_b}{Q_H + Cl_{int} \cdot fu_b}$$

$$F_H = \frac{Q_H}{Q_H + Cl_{int} \cdot fu_b}$$

$$Cl_{ren} = RBF \cdot E = GFR \cdot \frac{C_{in} - C_{out}}{C_{in}}$$

$$Cl_{ren} = \frac{\text{rate of excretion}}{\text{plasma concentration}}$$

$$Cl_{ren} = fu \cdot GFR + \left[\frac{\text{Rate of secretion - Rate of reabsorption}}{\text{Plasma concentration}}\right]$$

$$Cl_{ren} = \frac{\text{Urine flow} \cdot \text{urine concentration}}{\text{Plasma concentration}}$$

## Ideal Body Weight

**Male**
IBW = 50 kg + 2.3 kg for each inch over 5ft in height

**Female**
IBW = 45.5 kg + 2.3 kg for each inch over 5ft in height

**Obese**
ABW = IBW + 0.4*(TBW-IBW)

## Volume of Distribution

$$V = V_P + V_T \cdot K_P$$

$$V = V_P + V_T \cdot \frac{fu}{fu_T}$$

## Clearance

$$Cl = \frac{Dose}{AUC}$$

$$Cl = k_e \cdot V_d$$

## For One Compartment Body Model

| | | |
|---|---|---|
| **If the dosing involves the use of I.V. bolus administration:** | **For a single I.V. bolus administration:**<br>$$C_0 = \frac{D}{V}$$<br>$$C = C_0 \cdot e^{-k_e t}$$ | **For multiple I.V. bolus administration:**<br>$$Cn(t) = \frac{D}{V} \cdot \frac{\left(1 - e^{-nk_e\tau}\right)}{\left(1 - e^{-k_e\tau}\right)} \cdot e^{-k_e t}$$<br>at peak: t = 0; at steady state n→∞<br>at trough: t = τ<br>$$C_{\max ss} = \frac{D}{V} \cdot \frac{1}{(1 - e^{-k_e\tau})}$$<br>$$C_{\min ss} = C_{\max ss} \cdot e^{-k_e\tau}$$ |
| **If the dosing involves the use of I.V. infusion:** | **For a single short-term I.V. infusion:**<br>Since τ = t for $C_{max}$<br>$$C_{\max} = \frac{D}{Vk_eT} \cdot \left(1 - e^{-k_eT}\right)$$<br>$$C_{\min} = C_{\max} \cdot e^{-k_e(\tau - T)}$$ | **For multiple short-term I.V. infusion at steady state:**<br>$$C_{\max} = \frac{D}{Vk_eT} \cdot \frac{\left(1 - e^{-k_eT}\right)}{\left(1 - e^{-k_e\tau}\right)}$$<br>$$C_{\min} = C_{\max} \cdot e^{-k_e(\tau - T)}$$ |

Last modified 2010
C:\Current Data\pha5127_Dose_Opt_I\equations\5127-28-equations.doc

| | |
|---|---|
| **If the dosing involves a I.V. infusion (more equations):** | $C_t = \frac{D}{Vk_eT} \cdot \left(e^{k_eT} - 1\right) \cdot e^{-k_et}$ (most general eq.) during infusion t = T so,<br>$C_t = \frac{D}{Vk_eT} \cdot \left(1 - e^{-k_et}\right)$ (during infusion) at steady state $t \rightarrow \infty$, $e^{-k_et}$, $t \rightarrow 0$ so,<br>$Cpss = \frac{D}{Vk_eT} = \frac{k_0}{Vk_e} = \frac{k_0}{CL}$ (steady state) remembering $k_0 = \frac{D}{T}$ and<br>$CL = V \cdot k_e$ |
| **If the dosing involves oral administration:** | **For a single oral dose:**<br>$C = \frac{F \cdot D \cdot k_a}{V\left(k_a - k_e\right)} \cdot \left(e^{-k_et} - e^{-k_at}\right)$<br>$t_{\max} = \ln\left[\frac{k_a}{k_e}\right] \cdot \frac{1}{\left(k_a - k_e\right)}$<br>**For multiple oral doses:**<br>$C = \frac{F \cdot D \cdot k_a}{V\left(k_a - k_e\right)} \cdot \left[\frac{e^{-k_et}}{\left(1 - e^{-k_e\tau}\right)} - \frac{e^{-k_at}}{\left(1 - e^{-k_a\tau}\right)}\right]$<br>$t_{\max} = \ln\left[\frac{k_a \cdot \left(1 - e^{-k_e\tau}\right)}{k_e \cdot \left(1 - e^{-k_a\tau}\right)}\right] \cdot \frac{1}{\left(k_a - k_e\right)}$ |

Last modified 2010
C:\Current Data\pha5127_Dose_Opt_I\equations\5127-28-equations.doc