PHA 5127
Case Study 6
Fall 2007

SET I:
True or False

T F 1: For a multiple IV bolus regimen, if the dosing interval is the same, the shorter the half-life the more pronounced the differences between peak and trough concentrations. ***(T)***
$F=Cmax/Cmin=e^{(ke*\tau)}$

T F 2: For a multiple IV bolus regimen, the longer dosing interval, the longer it will take to achieve steady state. ***(F)***
Time to achieve steady state is about 5 half-lives.

T F 3: For a multiple IV bolus regimen, AUC at steady state within one dosing interval increases with the increase in dose***. (T)***
$AUC=Dose/CL$

T F 4: For a multiple IV bolus regimen, the accumulation degree is larger in patients with higher clearance. ***(F)***
$Rss=1/(1-e^{(-CL/V*\tau)})$

T F 5: It takes more time to reach steady state for a drug with a higher degree of accumulation. (Assuming loading dose is not given, and dosing interval is the same.) ***(T)***
$Rss=1/(1-e^{(-CL/V*\tau)})$*,higher Rss indicates longer half-life. Time to achieve steady state is about 5 half-lives.*

SET II:

A clinical study for drug X was conducted in 120 healthy volunteers. Drug X was given via IV bolus. The pharmacokinetics of Drug X can be described by linear one-compartment model. Volume of distribution of this drug is 13.3 L, and its half-life is 4 hr. If M.J was administrated this drug every 8hr (TID),

1. Calculate the accumulation factor at steady state.
   ke= Ln2/$T_{1/2}$=0.693/4= 0.173/hr
   *Rss=1/(1-exp(-ke*τ)=1/(1-exp(-0.173*8))=1.33*

2. Calculate the average concentration for a dose of 200mg.
   $\overline{C_{pss}}$ *=D/(CL*τ)=D/(ke*Vd*τ)=200/(0.1733*13.3*8)=10.85(mg/L)*

3. Calculate the maximum and minimum plasma concentrations (C_{max}, C_{min}) in the body at steady state if dose of 40mg.
   *C_{max}=D/Vd*Rss=40/13.3*1.33=4 mg/L*
   *C_{min}=Cmax*exp(-ke*τ)=4*exp(-0.173*8)=1 mg/L*

SET III:
For a multiple IV bolus regimen in a one-compartmental model, under following conditions,

a) Decrease clearance by two-fold

b) Increase volume of distribution by two-fold

c) Double each dose amount

d) Change dosing interval from twice a day (BID) to once a day (QD)

Discuss the change of the average steady-state concentration, the peak concentration, and the fluctuation

$$\overline{C_{ss}} = \frac{D}{Cl \bullet \tau}$$

$$C_{\max n} = \frac{D}{V_d} \bullet \frac{1 - e^{-n \bullet k_e \bullet \tau}}{1 - e^{-k_e \bullet \tau}}$$

$$C_{\max} = \frac{D}{V_d} \bullet \frac{1}{1 - e^{-k_e \bullet \tau}}$$

$$F = \frac{C_{\max}}{C_{\min}} = e^{K_e \bullet \tau}$$

scenarios	$C_{avg,ss}$	C_{max_ss}	F
a) CL↓ 2 folds	↑	↑	↓
b) V_d ↑ 2 folds	↔	↓	↓
c) D↑ 2 folds	↑	↑	↔
d) τ doubled ↑	↓	↓	↑