PHA5127 – Dose Optimization I
Case Study 1
Fall 2013

Question 1

Drug A was administered to a patient as an IV bolus at a dose of 250 mg. The pharmacokinetic parameters of the drug were clearance (CL) at 5.7 L/h, volume of distribution of the central compartment (V_c), 25 L. Assuming that the drug follows a one compartment body model with first order elimination, compute the following parameters (make sure to provide unit for each parameter in your answer):

(1) Estimate the elimination rate constant (k_e) and the half-life using the relationship $k_e = \frac{CL}{V_c}$.
(2) Compute the initial plasma drug concentration C_0.
(3) Compute the area under the curve $AUC_{0-\infty} = \frac{Dose}{CL}$
(4) Compute the concentration of the drug at 5 hour post dose if the doctor were to double the original dose.

Question 2

For the drug concentration-time profile below, you are given the following information. The route of drug administration was via IV bolus and the dose given was 20 mg.

Time (h)	Conc (ng/mL)
0	200
0.5	168
1	141
2	100
4	50
6	25
9	9
12	3

(1) Plot the plasma concentration versus time and determine the order of the elimination process.
(2) Determine k_e and half-life of the drug.
(3) Compute the clearance (CL) and volume of distribution (V_d)
(4) What are the expected concentrations of the drug at 14 h and 16 h?
(5) Use the trapezoidal rule to compute the $AUC_{0\text{-}12}$ of the profile above.

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True or False

(1) The plasma concentration time profile of a drug is not dependent of the dosage form.
(2) For a zero-order elimination process, the change in drug concentration with time is not a constant.
(3) The concentration-time profile of a one-compartment body model with first-order elimination after an IV bolus administration is a straight line in the semi-log scale.