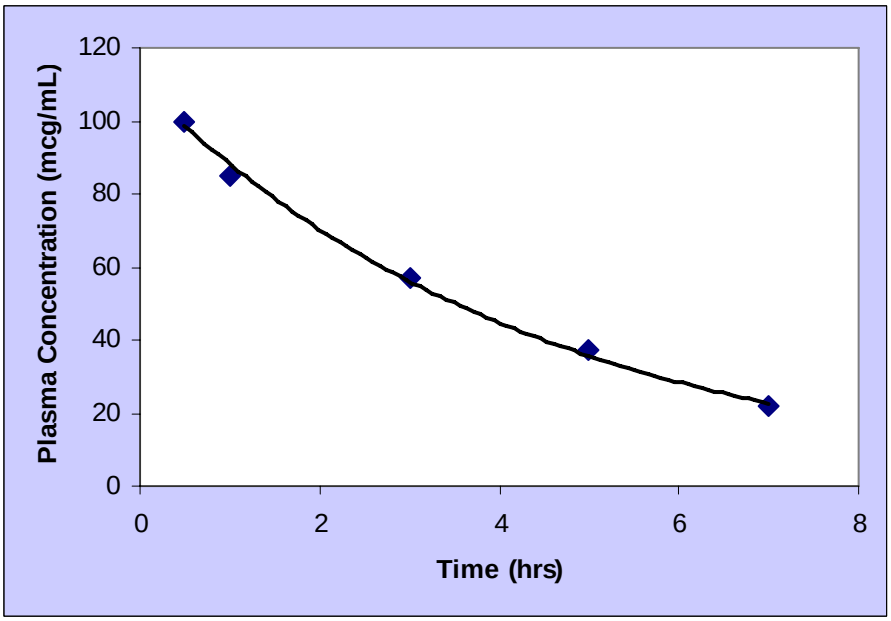
Case Study 1
PHA 5127 – Fall 2006
Revised 9/19/06

Question 1. A 3 year old, 15 kg patient was brought in for surgery and was given a 100 mcg/kg iv bolus injection of a muscle relaxant. The plasma concentrations were measured post injection and noted in the table below:

Time (h)	Plasma Conc. (mcg/L)
0.5	100
1	85
3	57
5	37
7	22

Determine the following pharmacokinetic parameters of the drug for this patient:

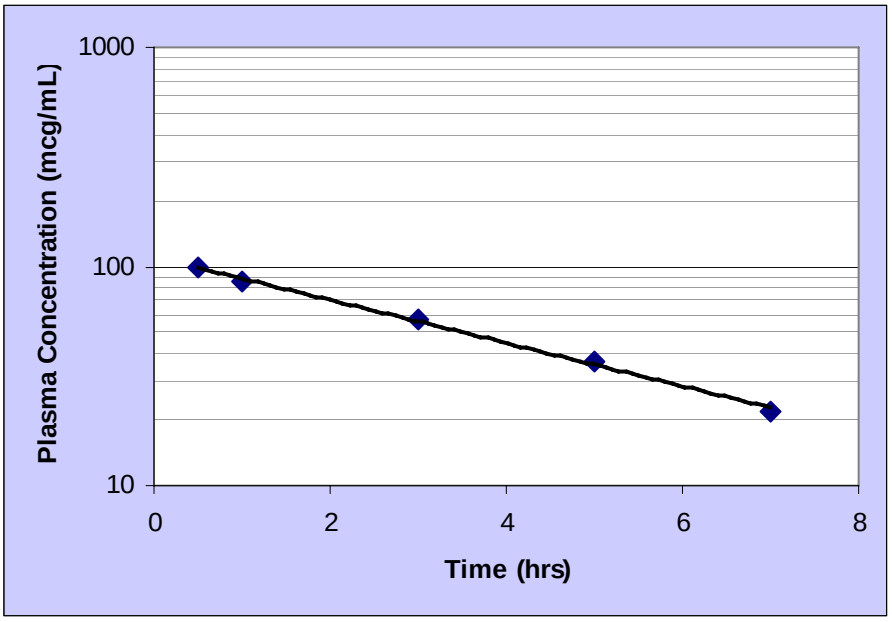
Before we begin to determine the pharmacokinetic parameters, we need to know what elimination process the drug is following. If we plot the data points from the table above, we would get the following:



Notice, we do not get a straight curve, so we cannot assume that the drug is following a zero order elimination process.

Case Study 1
PHA 5127 – Fall 2006
Revised 9/19/06

Let's plot the data on a semi-log scale:



Notice we do get a fairly straight line, so we can assume that this drug follows a first-order elimination process.

a) The elimination rate constant (k_e).
There are several ways to get k_e. The following just goes over two methods:

I. Plot the above data points on a semi-log paper (with time on the x-axis and plasma conc. on the y-axis) and draw a straight line thru the data points. Select two data sets on the line and plug into equation as shown below.
Say from the straight line, we get the concentration at 4 hrs which is 50 mcg/L and at 16 hrs which is 5 mcg/L.

$$k_e = \frac{\ln C_1 - \ln C_2}{t_2 - t_1} = \frac{\ln\left(50\,{}^{mcg}\!/\!_{L}\right) - \ln\left(5\,{}^{mcg}\!/\!_{L}\right)}{16hr - 4hr} = 0.2hr^{-1}$$

II. You can also use excel. Plot the time on the x-axis and the ln(Plasma Conc.) on the y-axis and put a trendline thru the data points. When you select the trendline option, you should also be able to get the equation of the trendline which in this case is

$$\ln(C) = -k_e \times t + \ln(C_o) = -0.2 \times t + 4.7$$

From this equation you get $k_e = 0.2\ hr^{-1}$

Case Study 1
PHA 5127 – Fall 2006
Revised 9/19/06

Please note, it usually is better to select data points from the trendline/line drawn to use for your calculations since the data may not always be perfect and fall on the trendline/best-fit-curve perfectly. This is why some people get two different k_e when selecting two different data sets straight from the table.

b) The half life ($t_{1/2}$).

$$t_{1/2} = \frac{\ln(2)}{k_e} = \frac{0.693}{k_e} = \frac{0.693}{0.2hr^{-1}} = 3.4hr$$

c) The initial plasma drug concentration (C_o).
Please note that the route of administration is i.v. bolus!
Again, there are several ways to get C_o. The following just goes over two methods:

I. Using the semi-log plotted method, extend the straight line thru the y-axis and the concentration at the y-axis, when t = 0 hrs, is C_0 which in this case is 110 mcg/L.
II. Using the trendline excel equation, you get $\ln(C_o) = 4.7$, so C_o =110 mcg/L.

d) The volume of distribution (V_d).

$$V_d = \frac{Dose}{C_0} = \frac{100\,mcg/kg \times 15kg}{110\,mcg/L} = \frac{1500mcg}{110\,mcg/L} = 13.6L$$

e) The area under the curve ($AUC_{0\rightarrow\infty}$) using the trapezoidal rule.
First start by getting the concentration at constant time intervals—say 0, 4, 8, 12, 16, and 20 hrs. You can the data points by i) reading them off the straight line plotted on the semi-log paper or ii) by using the trendline equation. The data points are as follows:

Time (hrs)	Concentration (mcg/L)
0	110
4	50
8	22
12	10
16	5
20	2

The calculations for AUC are as follows:

Case Study 1
PHA 5127 – Fall 2006
Revised 9/19/06

$$AUC_{t_1 \to t_2} = \frac{C_{t_2} + C_{t_1}}{2} \times (t_2 - t_1)$$

$$AUC_{0h \to 4h} = \frac{50\,{}^{mcg}\!/_{L} + 110\,{}^{mcg}\!/_{L}}{2} \times (4hr - 0hr) = 320\,{}^{mcg \cdot hr}\!/_{L}$$

$$AUC_{4h \to 8h} = 144\,{}^{mcg \cdot hr}\!/_{L}$$

$$AUC_{8h \to 12h} = 64\,{}^{mcg \cdot hr}\!/_{L}$$

$$AUC_{12h \to 16h} = 30\,{}^{mcg \cdot hr}\!/_{L}$$

$$AUC_{16h \to 20h} = 14\,{}^{mcg \cdot hr}\!/_{L}$$

$$AUC_{20h \to \infty} = \frac{C_{20h}}{k_e} = \frac{2\,{}^{mcg}\!/_{L}}{0.2hr^{-1}} = 10\,{}^{mcg \cdot hr}\!/_{L}$$

$$AUC_{0 \to \infty} = AUC_{0h \to 4h} + AUC_{4h \to 8h} + AUC_{12h \to 16h} + AUC_{16h \to 20h} + AUC_{20h \to \infty}$$
$$= (320 + 144 + 30 + 14 + 10)\,{}^{mcg \cdot hr}\!/_{L} = 582\,{}^{mcg \cdot hr}\!/_{L}$$

f) At 2 hours after injection, what is the plasma drug concentration?

$$C = C_0 \times e^{-k_e \times t} = 110\,{}^{mcg}\!/_{L} \times e^{-0.2^{hr^{-1}} \times 2hr} = 74\,{}^{mcg}\!/_{L}$$

Question 2. Following are the physicochemical properties of three drugs:

Property	Drug A	Drug B	Drug C
Molecular Weight	315	378	90,000
pKa	Neutral	Base	-
Polarity of unionized form	Non-polar	Polar	Protein

The muscle would most likely take up which of the above mentioned drugs? Why? What type of distribution (perfusion or permeability) limits the other drugs?

The muscle would most likely take up Drug A due to its small molecular weight and no charge. Permeability distribution limits the other drugs (i.e. the charge for Drug B and the high molecular weight for Drug C).

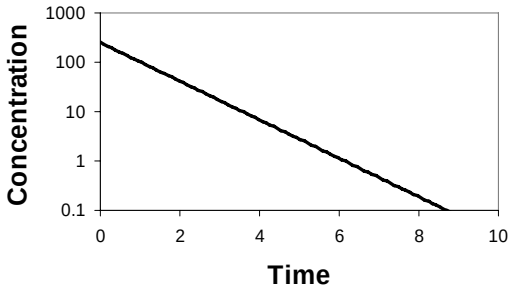
Case Study 1
PHA 5127 – Fall 2006
Revised 9/19/06

Question 3. Which of the following statements best describes a zero-order or first-order process:

a) The same fraction of drug is eliminated during a given time interval.
First-order. See slide 32 in ppt notes.

b) The same amount of drug is eliminated during a given time interval.
Zero-order. See slide 33 in ppt notes.

c) The time vs. plasma drug concentration profile is as follows:



First-order. Note that y-axis is on a semi-log scale.