Name: _____

UFID#: _____

PHA 5127

Final Exam
Fall 2004

On my honor, I have neither given nor received unauthorized aid in doing this assignment.

Name

Please transfer the answers onto the bubble sheet. The question number refers to the number on the bubble sheet. Please fill in all the information necessary to identify yourself. The proctors will also collect your exams.

Good LUCK.

Question/Points

TOTAL _____/140 pts will be adjusted later to 200 points per the syllabus

1 _____ /5 pts	11 _____ /6 pts	21 _____ /5 pts
2 _____ /5 pts	12 _____ /6 pts	22 _____ /5 pts
3 _____ /5 pts	13 _____ /5 pts	23 _____ /5 pts
4 _____ /5 pts	14 _____ /5 pts	24 _____ /5 pts
5 _____ /5 pts	15 _____ /5 pts	25 _____ /5 pts
6 _____ /5 pts	16 _____ /5 pts	26 _____ /5 pts
7 _____ /5 pts	17 _____ /5 pts	27 _____ /5 pts
8 _____ /5 pts	18 _____ /5 pts	28 _____ /2 pts
9 _____ /5 pts	19 _____ /5 pts	
10 _____ /6 pts	20 _____ /5 pts	

Name: _____

UFID#: _____

Question 1: Select the correct statement(s) concerning a two-compartment body model. (5pts)

1	For a two-compartment-body model drug, the rate constant describing the elimination of the drug from the central compartment (quantifying urinary and/or metabolic elimination) does not change with time after drug administration
2	The bi-exponential concentration time-profile, is due to the fact that clearance values change over time.
3	The two-compartmental behavior of a number of drugs is not the reason why peak-levels are often taken some time after stop of the drug administration
4	Let us assume that the toxicity of aminoglycosides is related to the drug-concentration in a deep peripheral compartment into which the drug enters very slowly and from which the drug leaves very slowly. Drug toxicity will be observed immediately after an iv bolus of this aminoglycoside.

The correct statement(s) is (are):

A: 1
B: 2 and 3
C: 1 and 4
D: 1 and 3
E: 1, 2 and 3

Name: _____

UFID#: _____

Question 2:

Select from the following statements the **correct** statement(s) (5pts)

1 The time to reach steady state differs for a drug dependent on whether the drug is given as a continuous constant rate infusion or whether a multiple dosing regimens (short-term infusions over a given time T, repeated at a given dosing interval) is used.

2 The time to reach steady state is determined by the half-life of the drug.

3 The time to reach steady state is affected by clearance and volume of distribution.

4 For multiple short term infusions, time to reach steady state depends on the dosing interval.

A: (1, 2, 3, 4)

B: (1, 2, 4)

C: (1, 3, 4)

D: (2, 3)

E: (2, 4)

Name: _____

UFID#: _____

Question 3-6:

The following applies to questions 3-6: A 60-kg patient is to be started on a **continuous intravenous infusion**. To achieve an immediate effect, a loading dose is to be administered over 30 min. (**given as short term infusion over 30 min)**, at which time the continuous infusion is started. From a previous regimen of the same drug, you estimate the patient's k_e is 0.07 h^{-1} and the V_d is 40 L. Assume that none of this drug has been administered this month.

Question 3: If the Cp_{ss} is to be 15 mg/L, what would be the loading dose (mg) given over 30 min? (5pts)

A 60 mg

B 120 mg

C 600 mg

D 610 mg

E 1220 mg

Name: _____

UFID#: _____

Question 4: What rate of infusion **(k_o for the following constant rate infusion**) should result in a Cp_{ss} of 15 mg/L (5pts)

A: $4.2\ hr^{-1}$

B: 42 mg/ 0.5 hours

C: 42 mg/hr

D: 42 mg

E: none of the above

Name: _____

UFID#: _____

Question 5: What will be the plasma concentration 12 hours after begin of the continuous infusion (Note that the loading dose is given over 30 minutes and the continuous infusion is directly started after the loading dose) (5pts)

A: 4.5 mg/L

B : 6.5 mg/L

C: 8.5 mg/L

D: 15 mg/L

E: None of the above.

Name: _____

UFID#: _____

Question 6: If the infusion is continued for 3 days and then discontinued, what would the plasma concentration be 12 hours after the stop of the infusion? Please perform calculations, we will check. (5 points)

A 1.2 mg/L

B: 6.5 mg/L

C: 7.5 mg/L

D: 15.0 mg/L

E: None of the above

Name: _____

UFID#: _____

Question 7: The infusion is continued for 3 days and the steady state concentration has been maintained at 15 mg/L. This infusion is stopped because the physician wants to increase the steady state concentration to 30 mg/L. What infusion rate is necessary to achieve this steady state concentration of 30 mg/L? Please perform calculations, we might check. (5 points)

A: 21 mg/L

B: 84 mg/0.5 h

C: 42 mg/0.5 h

D: 42 mg/h

E: None of the above.

Name: _____

UFID#: _____

The following pertains to Questions 8-9

A 60 kg patient is started on 80 mg of gentamycin, every 6 hr given as a one-hour infusion.

Question 8: If this patient is assumed to have an "average" volume of distribution (value of the population mean) of 0.25 L/kg and a normal half–life of 3 hr, what would be the peak plasma concentration at steady state (**C_{max} value observed 2 hours after the stop of the infusion**)? Please provide calculations. (5 points)

A: 3.2 mg/L

B: 8.9 mg/L

C: 12.2 mg/L

D: 15.4 mg/L

E: None of the above

Name: _____

UFID#: _____

Question 9: Based on the above volume of distribution and $t_{1/2}$ estimates, is the 6 hr dosing interval sufficient to achieve a fluctuation of at least 6? Please provide calculations. (5 points)

A: yes

B: no

C: Don't have enough information to make this conclusion.

Name: _____

UFID#: _____

Questions 10 -13

The following questions 10-13 are related to the equation shown below. Explain the meaning of the blocked parts of the equation in the following questions 10-13.

$$Cp_{min} = \boxed{\frac{k_o}{CL}} \bullet \frac{\boxed{1 - e^{-k_e * T}}}{1 - e^{-k_e \bullet \tau}} \boxed{\bullet e^{-k_e \bullet (\tau - T)}}$$

Question 10: What information does k_o/CL provide (5 points)

$$\frac{k_o}{Cl}$$

A: C_{max} after the first dose when given as iv infusion over the infusion time T.

B: Trough concentration at steady state when given as infusion.

C: C_{max} after the first dose when given as iv bolus injection.

D: Degree of accumulation.

E: Steady state levels of first infusion (concentration observed when first infusion would never stop).

Name: _____

UFID#: _____

Question 11: What does this part of the equation tells us (5 points)

$$\frac{1}{1-e^{-k_e \bullet \tau}}$$

A: Quantifies to what degree steady state has been achieved for the first constant rate infusion with T being the infusion time of a short term infusion.

B: Degree of accumulation observed at steady state when the drug is given as short term infusion with an infusion time T and a dosing interval tau.

C: C_{max} after the first dose when given as short-term infusion.

D: Allows the calculation of the trough concentration, without this part of the equation, one would obtain the true $C_{max.}$

Question 12: What does this part of the equation allows to calculate (5 points)

$$e^{-k_e \bullet (\tau - T)}$$

A: C_{max} after the first dose when given as an short-term iv infusion

B: Allows calculation of Trough concentration at steady state from peak levels after multiple short-term infusions.

C: C_{max} observed some time after the stop of the infusion (the nurses C_{max}, the one that will be send to the lab)

D: Degree of accumulation

E: Allows the calculation of the trough concentration after multiple iv bolus infusions, without this part of the equation, one would obtain $C_{max.}$

Name: _____

UFID#: _____

Question 13

For multiple iv bolus injection one can state (5 points)

1 that an increase in the dose (dosing interval stays the same) will increase the average steady state concentration.

2 that an increase in the dose will increase the trough concentration.

3 that an increase in the patient's clearance might necessitate a reduction of the patient's dosing interval.

4 that a reduction in the dosing interval (individual dose stays the same) will reduce fluctuation.

5 that a reduction in the dosing interval (individual dose stays the same) will increase peak levels observed at steady state.

Select the correct statements:

A: 1, 2, 3, 4

B: 1, 3, 4

C: 5

D: 1, 2, 3

E all of the above

Name: _____

UFID#: _____

Question 14-21: **Patient 1** received a **high extraction drug** as an iv bolus injection. Pharmacokinetic and physiological characteristics, such as dose, fraction of the drug unbound in plasma (fu) and tissue (fuT), volume of plasma (Vp) and volume of the tissue water (VTW) in this patient are shown below.

TABLE 1: INPUT PARAMETERS

	Patient 1
D [mg]	**40**
fu	**1**
fuT	**0.3**
Vp [L]	**3**
VTW [L]	**38**

Name: _____

UFID#: _____

The next table shows the resulting pharmacokinetic parameters in ~~this p~~**Patient 1**. Let's assume a second patient ~~will~~ receives the same dose of this drug, given ~~again~~ as an iv bolus injection. Both patients differ **only** in the plasma protein binding to this drug. As you can see from the INPUT parameters, 100% of the drug in plasma is free for **Patient 1. Contrary to this, in Patient 2, 50% of the drug present in plasma is free.**

Please circle in the free column of the Table 2 (**and in your Scantron**) for each parameter whether the parameter (Peak concentration, Ke, V, Cl, $t_{1/2}$, E, F, AUC) **will be larger (A), be about the same (B),or will be smaller (C)** than those estimates observed in **Patient 1**.

Table 2: OUTPUT PARAMETERS

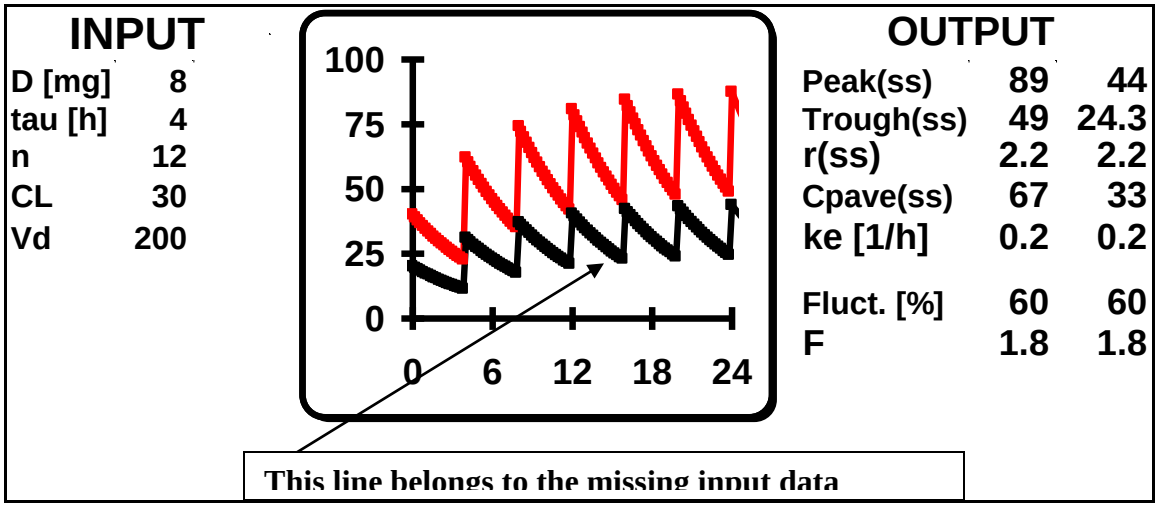
Question:		**Patient 1**	**Patient 2**
14 (5 points)	**V [L]**	**130**	Larger (A), same (B), Smaller (C)
15 (5 points)	**CL [L/h]**	**78**	Larger (A), same (B), Smaller (C)
16 (5 points)	**Peak [ug/ml]**	**0.3**	Larger (A), same (B), Smaller (C)
17 (5 points)	**Ke [1/h]**	**0.62**	Larger (A), same (B), Smaller (C)
18 (5 points)	**t1/2 [h]**	**1.1**	Larger (A), same (B), Smaller (C)
19 (5 points)	**E**	**0.97**	Larger (A), same (B), Smaller (C)
20 (5 points)	**F [%]**	**0.03**	Larger (A), same (B), Smaller (C)
21 (5 points)	**AUC [ug/ml*h]**	**0.51**	Larger (A), same (B), Smaller (C)

Name: _____

UFID#: _____

Question 22 :

The following concentration time profiles were observed after multiple bolus injections of a drug. The two curves differ in one of the input parameters (Dose, CL or Vd). (5 points).



+

Identify the one input parameter that differs

A: Dose

B: Clearance

C: Volume of distribution

D: tau

E: none of the above

Name: _____

UFID#: _____

Question 23:

Which of the following factors significantly affect(s) the renal clearance of a unionized drug that shows “complete” passive renal reabsorption from the “urine” back into the blood: (5 pts)

1. plasma protein binding.
2. activity of cationic transporters in the tubuli.
3. urine flow.
4. pH of urine.
5. liver blood flow.

A: 1, 2, 3,

B: 1, 3,

C: 1, 3, 4, 5,

D: 1, 3, 5,

E: none of the above combinations.

Name: _____

UFID#: _____

Questions 24- 28

Mark whether the following statements are true (A) or false (B).

Question 24 (5 points)

T (A) F (B) Loading doses are mainly given for drugs with high k_e values

Question 25 (5 points)

T (A) F (B) A large volume of distribution during the elimination phase of a two-compartment body model might be due to the high metabolic clearance of this drug.

Question 26 (5 points)

T (A) F (B) "Linear pharmacokinetics" means that the plasma drug concentration versus time plots will result in a straight line.

Question 27 (5 points)

T (A) F (B) The dosing interval for multiple short term infusions is determined by the desired fluctuation, the half-life of the drug and the time over which the infusion is given.

Question 28 (2 points) (Bonus Question)

T (A) F (B) I hate Dose-Op.