

## PHA 5127 Dose Optimization I

### Homework III (10 points)

Due on Friday, 09/24/2010

1. A patient was given 800mg of a high extraction drug as an IV bolus injection and plasma concentration dropped from peak concentration of 2 mg/L with a rate constant of  $0.2 \text{ h}^{-1}$ . (4 point)

(1) Estimate the hepatic clearance and  $AUC_{\infty}$ . (Assume there are only hepatic and renal clearance, and renal clearance of this patient is 8L/h)

(2) If the fraction unbound in plasma increases two fold, please determine the oral bioavailability of this drug. (Assume the liver blood flow of this patient is 80L/h and there is no other physiological change.)

2. Please predict changes on the pharmacokinetic parameters for a drug that is eliminated only through hepatic clearance after physiological changes happen ( $\uparrow$ ,  $\downarrow$ ,  $\leftrightarrow$  indicate increase, decrease and same): (0.25 point for each, 6 point)

Scenarios	High extraction drug			Low extraction drug		
	CL	F	$t_{1/2}$	CL	F	$t_{1/2}$
Increase in plasma protein binding						N/A
Increase in tissue binding						
Increase in liver blood flow						
Decrease in liver enzyme activity						