PHA 5127 Dose Optimization I
Fall 2011
Case Study IV

If you have any questions regarding this case study, do not hesitate to contact Benjamin Weber (benjaminweber@ufl.edu). Please remember that attendance is mandatory. Students whose IPEE coincides with the case study lecture are excused.

Problem 1

T.T. (male, 6'3'' tall, 111 kg, 24 years old) shows a serum creatinine level of 1.3 mg/dL.

a) Use the Cockcroft-Gault-Equation to calculate his creatinine clearance and glomerular filtration rate (GFR). Comment on the renal function of T.T.?
b) Why do we use the creatinine clearance to estimate the GFR?
c) Drug A shows a plasma protein binding and tissue protein binding of 10% and 95%, respectively. Drug A is eliminated by hepatic (80%) and renal processes (20%). Calculate the total systemic clearance of drug A (in L/h) when administered to T.T.Assume that the drug is neither actively secreted nor reabsorbed.
d) Graph the plasma-concentration time profile for the first 24 hours when 1000mg of drug A are administered to T.T. via an IV bolus injection. Assume that the drug is immediately distributed throughout the body, crosses membranes easily, and that all elimination processes are first-order processes.

Problem 2

Which properties does a drug need to have in order to demonstrate the following? Explain briefly.

a) Active tubular secretion
b) Glomerula secretion
c) Passive tubular reabsorption

Problem 3

Assume that drug B is only cleared by metabolism processes. For a fixed VD, sketch graphs describing the relationship between the following PK metrics for a) non-saturable metabolism enzymes (linear PK) and b) saturable metabolism enzymes (non-linear PK).

I. dX/dt (elimination rate) vs. C (plasma concentration)
II. CL vs. Dose
III. AUC vs. Dose