The USC Laboratory of Applied Pharmacokinetics presents a Workshop on

Population Pharmacokinetic/Dynamic Modeling: Basic Concepts and Clinical Applications to Optimally Individualized Drug Therapy.

Wednesday & Thursday, May 7-8, 2003

This course is for physicians and pharmacists with an interest in population pharmacokinetic/dynamic modeling who have a grasp of the basic aspects of such work. **Day 1** will introduce and review **Basic PK/PD tools and concepts** of pharmacokinetic modeling, and will emphasize their application to optimal patient care. **Day 2** will discuss intermediate and advanced **PK/PD tools, and concepts,** including parametric and nonparametric population modeling. **Note:** if you would like to bring your own laptop computer to obtain and learn the relevant software (not included in the registration fee), you are encouraged to do so.

Preliminary Program

Faculty:
***Roger Jelliffe, M.D.**, Professor of Medicine, USC School of Medicine, USA*
***Irina Bondareva, Ph.D.,** Institute for Physical and Chemical Medicine, Moscow, Russia*
***Dimiter Terziivanov, M.D**., Hospital St. J. Rilsky, Sofia, Bulgaria*

Wednesday, May 7, 2003 – Pharmacokinetics and Optimal Patient Care

8:30 AM - Registration
9:00 AM - Welcome - Dr. Terziivanov
9:15 AM - Review of Basic Pharmacokinetic Concepts - Dr. Bondareva
- Compartmental Models
  - Cumulation and Elimination
  - T ½, Fraction lost, Doses sustained.
  - Changing T ½, changing dose, outcomes.

9:45 AM – Ways of fitting data for patients
- Linear regression of logs of data
  - Must wait for steady state
  - Must wait for complete distribution after a dose
- Nonlinear regression on the data itself
  - No wait for steady state
  - No wait for distribution
- Bayesian fitting – the best
- The MAP Bayesian scenario and feedback strategy

10:30 AM - Break

10:45 AM - Estimation of Creatinine Clearance without a urine specimen in unstable patients – Dr. Jelliffe
11:00 AM - When to obtain serum data – Dr. Jelliffe
- Not just the trough
- Capture the dynamics
- Some optimal strategies

11:20 AM - Modeling the assay error – Dr. Bondareva
11:40 AM - Parametric population models – Dr. Bondareva
- What "parametric" means here
- The iterative Bayesian (IT2B) modeling approach
  - Separating inter - from intra-individual variability (IIV)
  - Separating IIV from assay error
- Demonstration of the approach – an Amikacin data set

12:00 Noon - Nonparametric population modeling approaches – Dr. Jelliffe
- What "nonparametric means here
- The NPEM approach
- Using IIV, assay error, and stated ranges

12:15 PM - Using population modeling approaches optimally – Dr. Jelliffe
- Get the assay error polynomial
- Use IT2B - get Gamma
- Then use NPEM, get the entire joint density, essentially resolving the population into up to one model for each subject studied.

12:30 PM - Lunch

1:30 PM - The separation principle: limitations to current dosage methods – Dr. Jelliffe
1:45 PM - Introduction to multiple model (MM) dosage design – Dr. Jelliffe
- Software for MM dosage regimens

2:15 PM - Getting MM Bayesian posterior joint densities – Dr. Jelliffe
- MM Bayesian posteriors
- A new method – IMM – for detecting changing parameter values in patients

2:40 PM - How to plan and develop individualized dosage regimens for patients – Dr. Jelliffe
- Set a target goal for each patient according to the need for the drug.
- Aminoglycosides 10 and 1, or 20 and 0.5
- Vancomycin trough 10
- Digoxin – really a 2 compartment model
  - Clinical effect correlates better with tissue than serum concentrations
  - How to manage this problem clinically
  - Serum troughs 0.9 ng/ml
  - Peripheral peaks 7.0 ug/kg
  - Patients with atrial fibrillation need more

3:00 PM - Case studies in aminoglycoside therapy
- Therapeutic drug monitoring
- Making the individualized, Bayesian posterior, model
  - Analyzing the data
  - A patient on dialysis

3:30 PM - Break

3:45 PM – Modeling Caffeine Metabolism and its Genetic Components – Dr. Terziivanov
4:15 PM – Concentration versus time-dependent drugs: Modeling organism growth and kill – Dr.Jelliffe
4:45 PM - Adjourn

Thursday May 8, 2003 –Modeling Tools and Applications

9:00 AM - Cost-effectiveness of optimal aminoglycoside therapy – Dr. Jellliffe
9:30 AM - Outcomes in Busulfan therapy for bone marrow transplants in children – Dr. Jelliffe
9:45 AM - Case studies in digoxin therapy
An initial regimen for a patient with atrial fibrillation
A case history: another patient with atrial fibrillation
A patient on digoxin and quinidine
10:10 AM – Case studies in Aminoglycoside therapy – Dr. Jellliffe
A Patient on Gentamicin
A dialysis patient on Gentamicin
A difficult patient on Tobramycin

10:30 AM – Break

10:45 AM – Demo – Making an IT2B population model of Amikacin – Dr. Jelliffe
11:20 AM – Demo – Making a NPAG population model of Amikacin – Dr. Jelliffe
12:00 Noon – Comparing results: parametric and Nonparametric models – Dr.Jelliffe

12:30 PM - Lunch

1:30 PM - 3:45 PM - Modeling of Antiepileptic Drugs - Dr. Bondareva
2:00 PM - Making large and nonlinear population models – Dr. Bondareva
Demo - Using BOXES making a Michaelis-Menten model of Phenytoin
2:15 PM - Demo setting up Big NPAG Model. Modelling Phenytoin - Dr. Bondareva
A typical subject data file
Setting up the model, the data, the instructions, sending it, analysing it. Evaluating the results

3:00 PM - BREAK

3:30 PM – Summary: Strengths and Weaknesses of Parametric and Nonparametric methods – Dr. Jelliffe

4:00 PM – Adjourn.