A 3-DAY INTRODUCTORY WORKSHOP IN POPULATION PK DATA ANALYSIS WITH NONMEM®

University at Buffalo School of Pharmacy and Pharmaceutical Sciences

A HANDS-ON COURSE USING NONMEM®
Thursday, August 27– Saturday, August 29, 2020
Niagara Falls, NY

Cognigen
A SIMULATIONS PLUS COMPANY

WORKSHOP SYNOPSIS

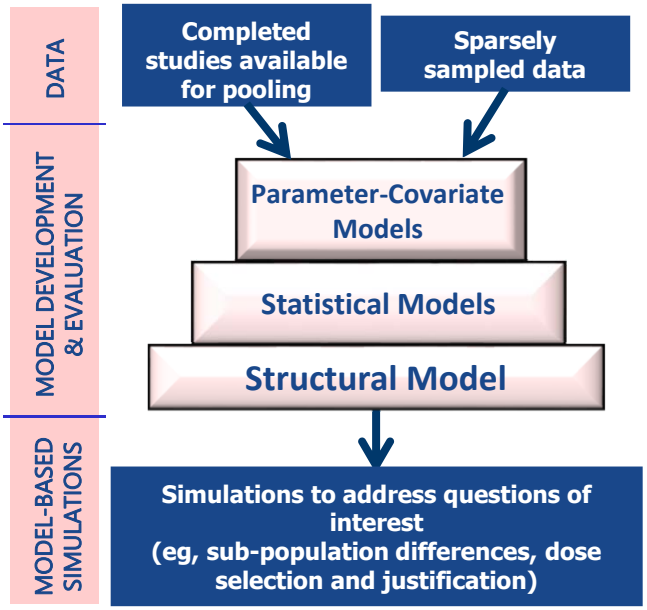
This introductory population PK training workshop has been designed to provide the necessary information to successfully implement population pharmacokinetic methodology in a drug development program and to provide the foundation for understanding the basics of NONMEM coding and interpretation of NONMEM output. The material is structured to impart both the theoretical and practical aspects of the population approach and is versatile so that participants with diverse backgrounds and areas of expertise may benefit. Examples of the use of population PK studies in drug development programs will be presented to provide specific details of various implementations and better illustrate essential aspects of population PK methods. Participants will gain an appreciation for the essentials of accurate and sufficient data collection and learn how to proactively plan in order to maximize study effectiveness. Throughout the workshop, the presenters will provide examples from their experience to inform best practices for implementation and avoiding problems. Emphasis will be placed on compliance with the FDA's Guidance for Industry on Population PK and the EMA's Guideline on Reporting the Results of Population PK Analyses.

The workshop content is provided as a combination of formal lectures, review of data, code, and data analysis results, in addition to hands-on exercises. Participants will use their own laptop computers, with which they will be able to practice coding control streams, running various models, and evaluating the results. A thorough examination of an example dataset, from development of the structural and statistical models through covariate analysis will be covered. To ease the learning curve and ensure that participants are up and running with NONMEM very quickly, the KIWI™ Pharmacometric Communication Platform will be used in conjunction with NONMEM. KIWI is useful in facilitating code writing, finding errors, comparing output from different models, and generating point-and-click model diagnostics.

LEARNING OBJECTIVES

Following the workshop, the participant should be able to:

1. Understand the conceptual basis and rationale for the population approach to data analysis, its benefits and advantages, including where and when population methods may be optimally applied during drug development
2. Write, execute, and de-bug basic NONMEM® control streams for structural PK models
3. Outline the requirements and understand the format for basic NONMEM® datasets
4. Understand the importance of exploratory data analysis (EDA) and the interpretation of standard goodness-of-fit diagnostic plots
5. Perform covariate analyses to evaluate determinants of variability by understanding, identifying, and coding basic functional forms for covariate-parameter relationships
6. Understand the basis for model selection strategies and discriminate between candidate models on the basis of both quantitative and qualitative factors
7. Understand and interpret NONMEM® output, including error messages, and have insight into potential model refinement issues



COURSE INSTRUCTION

The workshop is organized and taught by experienced pharmacometricians from Cognigen Corporation, also affiliated with the University at Buffalo and Union University Departments of Pharmaceutical Sciences. Cognigen Corporation, a wholly owned subsidiary of Simulations Plus, Inc., has been providing clinical pharmacology and pharmacometric consulting services, including population PK/PD modeling and simulation to the global pharmaceutical industry for over 25 years to generate and communicate the knowledge required for time-sensitive decision-making and regulatory review. The workshop will be primarily taught by Jill Fiedler-Kelly and Joel Owen, co-authors of *Introduction to Population Pharmacokinetic/Pharmacodynamic Analysis with Nonlinear Mixed Effects Models* (John Wiley & Sons Inc., 2014).

Jill Fiedler-Kelly

Joel Owen

This session is followed by a 3-day separate course in the concepts and applications of Pharmacokinetic/Pharmacodynamic Modeling coordinated by Dr. William J. Jusko. For information see: http://pharmsci.buffalo.edu/ or contact Suzette Mis at mis@buffalo.edu.

AGENDA

Thursday, August 27, 2020

08:00-08:35	Continental Breakfast
08:35-08:45	**Welcome and Introduction to the Workshop**
08:45-09:45	**The Population Approach in Drug Development**
09:45-10:20	**Population Modeling Basics**
10:20-10:40	Break
10:40-11:50	**NONMEM® Terminology**
11:50-12:45	**Estimation Methods in NONMEM®**
12:45-01:45	Lunch
01:45-03:15	**Brief Overview of the NONMEM® Program and Writing an NM-TRAN Control Stream**
03:15-03:35	Break
03:35-04:05	**NM-TRAN Lecture (cont'd)**
04:05-05:20	**NONMEM® Dataset Structure**
05:20-05:30	**Exercise: Writing Control Streams and Diagnosing Dataset Problems**

Friday, August 28, 2020

08:00-08:30	Continental Breakfast
08:30-09:15	**Discuss Control Stream and Dataset Exercise**
09:15-09:50	**Exploratory Data Analysis**
09:50-10:20	**Exercise: Introduction to KIWI**
10:20-10:40	Break
10:40-11:25	**Running NONMEM® and Interpreting the Output**
11:25-11:35	**Data Review: Introduction to the Example Dataset and Exploratory Data Analysis**
11:35-12:30	**Exercise: Developing a Base Structural Model**
12:30-01:30	Lunch
01:30-02:00	**Base Structural Model Exercise (cont'd)**

Friday, August 28, 2020 (con't)

02:00-02:10	**Data Review: Base Model**
02:10-02:45	**Model Diagnostic Plots**
02:45-03:05	Break
03:05-03:35	**Model Selection and Covariate Evaluation – Part 1: The Covariate Assessment Process**
03:35-04:25	**Covariate Evaluation–Part 2: Functional Forms**
04:25-04:40	**Data Review: Introduction to Covariate Analysis and Coding Issues**
04:40-05:30	**Exercise: Forward Selection of Covariate Effects**

Saturday, August 29, 2020

08:00-08:30	Continental Breakfast
08:30 -09:00	**Forward Selection Exercise (cont'd)**
09:00-09:40	**Data Review: Forward Selection Results and Multivariable Model Checking**
09:40-10:20	**Exercise: Backward Elimination of Covariate Effects**
10:20-10:40	Break
10:40-11:20	**Backward Elimination Exercise (cont'd)**
11:20-12:00	**Applications of Bayesian Parameter Estimation**
12:00-01:00	Lunch
01:00-02:50	**Diagnosing Errors, Model Checking, Model Refinement, and Model Evaluation Techniques**
02:50-03:00	**Data Review: Backward Elim & Model Refinement**
03:00-03:20	Break
03:20-03:40	**Pharmacometric Analysis Planning and Population PK/PD Modeling and Simulation**
04:20-04:30	**Wrap-up and Final Q & A**

REGISTRATION DETAILS

Course location: The course will be held at The Conference & Event Center Niagara Falls, 101 Old Falls Street, Niagara Falls, NY 14303. USA. Phone: (716) 278-2100. Fax: (716) 278-0008. The Conference Center is 28 minutes from the Buffalo Niagara International Airport. Website: http://www.ccnfny.com.

Hotel location: *Sheraton Niagara Falls*, 300 Third Street, Niagara Falls, NY 14303. USA. Phone: (716) 285-3361. The price is $124/night August & $96/night September single/double occupancy (triple/quadruple add $10 per person). *Hotel Deadline: July 31st, 2020.*
Website: https://book.passkey.com/go/2020PKPDModeling

Fee: The fee is $2800. Graduate student rate of $1400 is available for up to 3 participants. The registration fee includes hard-copy course documentation, USB drive with code examples, and a copy of the textbook, *Introduction to Population Pharmacokinetic/Pharmacodynamic Analysis with Nonlinear Mixed Effects Models* by Owen and Fiedler-Kelly (John Wiley & Sons Inc., 2014). Continental breakfasts, lunches and break-time refreshments during the course are included. No walk-ins accepted.

Requirements: Laptop computers equipped with Google Chrome with Flash 9+ plugins are required to fully participate in hands-on exercises. Access to NONMEM and KIWI will be provided for the duration of the course.

Registration: Online registration will begin April 30th, 2020. The course is limited to the capacity of 25 participants. Confirmation email of registration will be returned upon successful registration at the following website: http://pharmacy.buffalo.edu/ under Quick Links.

Cancellations: Cancellations with a full refund may be made until July 6, 2020. No refunds will be given for cancellations received after this date. Substitutions may be made at any time.

Payment: Mastercard, Visa, American Express, and Discover card payments will be accepted only at the following website: http://pharmacy.buffalo.edu/ under Quick Links. Contact UB course secretary: Suzette Mis, (716) 645-4831; mis@buffalo.edu, if you need further assistance.

Social Activities: An evening dinner outing, sponsored by Cognigen Corporation, will be offered on Thurs., Aug. 27th .