AN INTRODUCTORY WORKSHOP in POPULATION PK DATA ANALYSIS with NONMEM®

University at Buffalo School of Pharmacy and Pharmaceutical Sciences

HANDS-ON COURSE USING NONMEM®
Thursday, May 12 – Saturday, May 14, 2022
Niagara Falls, NY

SimulationsPlus
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WORKSHOP SYNOPSIS

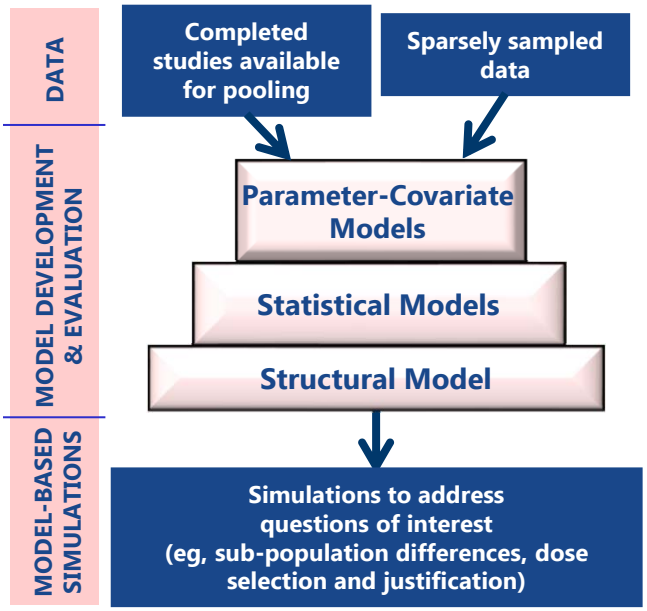
This introductory population PK training workshop has been designed to provide the necessary information to successfully implement population pharmacokinetic methodology in a drug development program and to provide foundational understanding of **the basics of NONMEM coding** and **interpretation of 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. *No prior experience with NONMEM is assumed or required.* 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 will be provided as a combination of **live lectures, review of data, code, and modeling results, plus hands-on individual and small group exercises**. Participants 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 model refinement issues



COURSE INSTRUCTION

The workshop is organized and taught by experienced pharmacometricians from the Cognigen division of Simulations Plus, Inc., also affiliated with the University at Buffalo and Union University Departments of Pharmaceutical Sciences. The Cognigen division of Simulations Plus 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. In addition to other instructors, the workshop will feature Luann Phillips, as well as 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

AGENDA

Thursday, May 12, 2022

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, May 13, 2022

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, May 13, 2022 (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, May 14, 2022

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 Center is 28 min from Buffalo International Airport. Website: http://www.ccnfny.com

Accommodations: Several nearby hotels within walking distance are available. Please book directly as soon as registered for this course. Possible hotels: Sheraton Niagara Falls, Quality Hotel & Suites At The Falls, Hyatt Place Niagara Falls, Wingate by Wyndham Niagara Falls, Comfort Inn The Pointe, The Cadence, Seneca Niagara Resort & Casino, Holiday Inn Niagara Falls-Scenic Downtown, Wingate by Wyndham Niagara Falls, The Giacomo, and others.

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 **January 24th, 2022**. The course is limited to the capacity of 30 participants. Confirmation email of registration will be returned upon successful registration at the following web site: http://pharmacy.buffalo.edu/ under Quick Links.

Cancellations: Cancellations with a full refund may be made until **March 14th, 2022**. No refund is possible on 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 course secretary: Suzette Mis, (716) 645-4831; mis@buffalo.edu, if you need further assistance.

COVID STATEMENT: Masks must be worn for in-person classes and hands-on training. The University at Buffalo, Simulations Plus - Cognigen Division, The Convention & Event Center Niagara Falls, and hotels are not liable for any COVID-19 related issues. Proper protocols must be followed. Full vaccination is highly recommended. Rigorous cleaning protocols are performed.

This session precedes two separate courses: a PK/PD Modeling course and a Monoclonal Antibody PK/PD course, coordinated by Drs. Joseph Balthasar, Dhaval Shah, Donald Mager, and David D'Argenio. For information see: http://pharmacy.buffalo.edu/ or contact Suzette Mis at mis@buffalo.edu.