A Virtual Introductory Workshop in Population PK Data Analysis

September 25th – October 6th, 2023

Jill Fiedler-Kelly **Luann Phillips**

Virtual Hands-On Course Using NONMEM®

Dates: September 25th – October 6th, 2023

Sessions on Monday, Wednesday, and Friday only

Time: 12:30 PM to 4:30 PM ET, USA

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
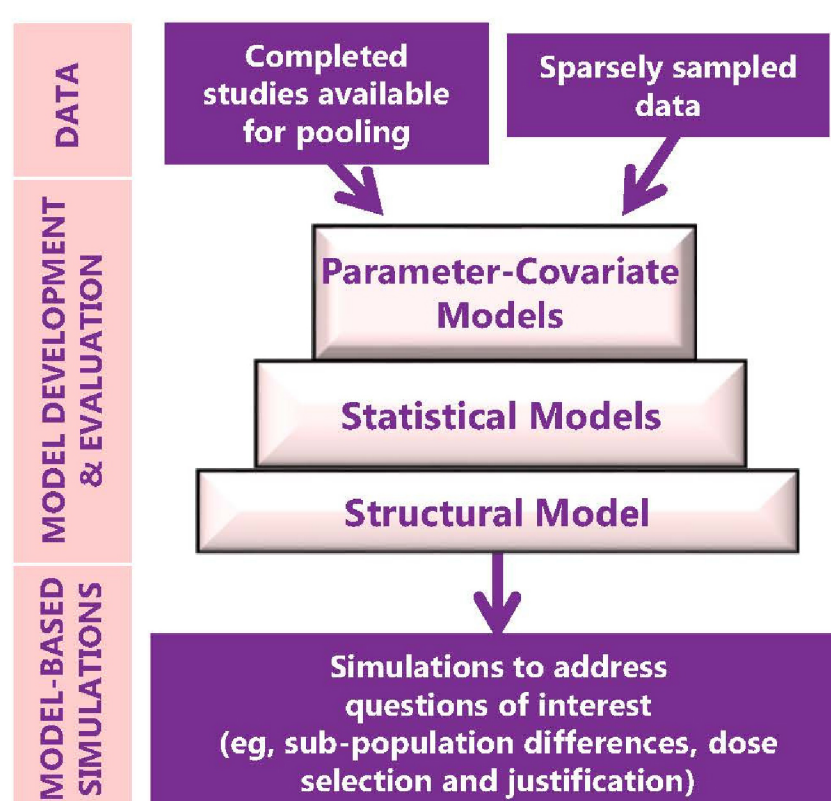
Course Instruction

The workshop is organized and taught by experienced pharmacometricians from the Cognigen division of Simulations Plus, Inc., also affiliated with the University at Buffalo. The Cognigen division 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. In addition to other instructors, the workshop will feature Luann Phillips, as well as Jill Fiedler-Kelly, co-author of Introduction to Population Pharmacokinetic/Pharmacodynamic Analysis with Nonlinear Mixed Effects Models (John Wiley & Sons Inc., 2014).

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Agenda (Times in EST)

Monday - September 25th

12:30 - 12:40   **Introduction and Welcome**

12:40 - 13:40   **Lecture 1: The Population Approach in Drug Development**

13:40 - 14:15   **Lecture 2: Population Modeling Basics**

14:15 - 14:30   ***Break***

14:30 - 16:05   **Lecture 3: NONMEM® Terminology and Classical Estimation Methods**

16:05 - 16:30   **Lecture 4: Brief Overview of the NONMEM® Program and Writing an NM-TRAN Control Stream (PART 1)**

Wednesday - September 27th

12:30 - 14:20   **Lecture 4: Brief Overview of the NONMEM® Program and Writing an NM-TRAN Control Stream (PART 2)**

14:20 - 14:35   ***Break***

14:35 - 15:45   **Lecture 5: NONMEM® Dataset Structure**

15:45 - 16:15   **Exercise 1: Writing Control Streams and Diagnosing Dataset Problems**

16:15 - 16:30   **Questions**

Friday - September 29th

12:30 - 13:15   **Review Exercise 1**

13:15 - 13:45   **Lecture 6: Exploratory Data Analysis**

13:45 - 14:00   ***Break***

14:00 - 14:45   **Lecture 7: Running NONMEM® and Interpreting the Output**

14:45 - 15:20   **Exercise 2: Introduction to KIWI**

15:20 - 15:30   **Data Review 1: Introduction to Example Dataset and Exploratory Data Analysis**

15:30 - 16:30   **Exercise 3: Developing a Base Structural Model (Part 1)**

Monday - October 2nd

12:30 - 12:55   **Exercise 3: Developing a Base Structural Model (Part 2)**

12:55 - 13:10   **Data Review 2: Base Model**

13:10 - 13:45   **Lecture 8: Model Diagnostic Plots**

13:45 - 14:15   **Lecture 9: Model Selection and Covariate Evaluation – Part 1: The Covariate Assessment Process**

14:15 - 14:30   ***Break***

14:30 - 15:20   **Lecture 10: Covariate Evaluation – Part 2: Functional Forms & Coding Issues**

15:20 - 15:35   **Data Review 3: Introduction to Covariate Analysis**

15:35 - 16:30   **Exercise 4: Forward Selection of Covariate Effects**

Wednesday - October 4th

12:30 - 12:55   **Exercise 4: Forward Selection of Covariate Effects (cont'd)**

12:55 - 13:35   **Data Review 4: Forward Selection Results and Multivariable Model Checking**

13:35 - 14:30   **Exercise 5: Backward Elimination of Covariate Effects**

14:30 - 14:45   ***Break***

14:45 - 15:10   **Exercise 5: Backward Elimination of Covariate Effects (cont'd)**

15:10 - 15:25   **Data Review 5: Backward Elimination**

15:25 - 16:05   **Lecture 11: Applications of Bayesian Parameter Estimation**

16:05 - 16:30   **Lecture 12: Diagnosing Errors, Model Checking, Model Refinement and Model Evaluation Techniques (PART 1)**

Friday - October 6th

12:30 - 14:05   **Lecture 12: Diagnosing Errors, Model Checking, Model Refinement and Model Evaluation Techniques (PART 2)**

14:05 - 14:20   ***Break***

14:20 - 15:45   **Lecture 13: Pharmacometric Analysis Planning, Population PK/PD Modeling and Simulation Examples**

15:45 - 16:15   **Review of Example Analysis (Perspective Map)**

16:15 - 16:30   **Wrap-up and Final Q&A**

Course location: The course will be conducted virtually.

Fee: The fee is $3,000. Graduate student rate of $1500 per student (limit of 5 students). The registration fee includes access to the course documentation, code examples, and complete details of an example analysis.

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