

**MI210-W: Essentials of Population PK-PD Modeling & Simulation (3 CR)**

MI210 provides an extensive overview of topics in population pharmacokinetics and pharmacodynamics, including nonlinear mixed-effects modeling theory and implementation, data formatting requirements, population model development, model evaluation techniques, continuous PK-PD models, Monte Carlo simulation, and best practices. Instruction combines didactic lectures with hands-on exercises using R, Mifuns, and the NONMEM<sup>®</sup> 7 software. Participants may apply the 3 credit hours from this course to the Metrum Institute Certificate Program in Pharmacometrics.

**Instructors**

Marc Gastonguay and Metrum Institute staff

**Prerequisites**

Basic understanding of pharmacokinetic and pharmacodynamic principles, compartmental pharmacokinetic models, introductory statistics, familiarity with the R or S language. Applicable MI Courses include: MI120, MI101, MI201, or contact us: [info@metruminstitute.org](mailto:info@metruminstitute.org).

**Computer Hardware/Software**

This course requires a Windows computer with a web browser. Students will be given access to a Metrum Institute web-application server for hands-on examples including all required software. Details on how to access the program are provided at the start of the course.

**Spring 2010 Schedule**

March	16, 19, 23, 26, 30
April	2, 6, 9, 13, 16, 20, 23, 27, 30
May	4, 7, 11, 14, 18, 21, 25, 28
June	1, 4, 8, 11, 15, 18

Tuesdays 2–4 pm Eastern Time (lecture)

Fridays 2–3 pm Eastern Time (lab)

**Location**

Live webcast

**Fees**

Regular registration: \$3000 USD / Academic & government registration: \$1500 USD

**Course Outline**

1. Introduction to nonlinear regression and nonlinear mixed-effects models
  - Nonlinear mixed-effects modeling
  - Population modeling methods in NONMEM<sup>®</sup> 7
  - Population model diagnostics
  - Exercise: build your own LS objective function
2. Data requirements for NMTRAN
  - Types of data in population PK-PD
  - Introduction to NONMEM<sup>®</sup> 7 system
  - NMTRAN requirements and specifications
  - Data specification document
  - Exercise: estimate parameters for a population PK model
3. Individual and population PK models
  - Coding pharmaco-statistical models through NMTRAN
  - Covariance matrix structure
  - Interpreting NONMEM<sup>®</sup> output
  - Goodness-of-fit diagnostics
  - Comparing alternative models
  - Individual vs. population PK parameter estimates
  - Exercise: estimate parameter estimates for a population PK model
4. Covariate model building
  - Types of covariate-parameter relationships
  - Before you start model building
  - Statistical considerations
  - Model-based inferences

- Exercise: explore covariate effects on a population PK model
5. Basic models for continuous PK-PD
    - Population PK-PD data
    - Direct population PK-PD models
    - Effect-compartment models
    - Exercise: model population PK-PD systems
  6. Monte Carlo simulation of population PK-PD systems
    - Utility of simulation
    - Advantages of simulation in NONMEM<sup>®</sup>
    - Coding of NMTRAN control stream and data template
    - Monte Carlo simulation
    - Individual data
    - Population data
    - Uncertainty and variability
    - Exercise: simulate expected PK study outcome
  7. Population PK-PD model evaluation
    - Rationale for model evaluation
    - Risk-based approach
    - Assumption checking
    - Evaluation methods
    - Prediction errors
    - Cross-validation
    - Bootstrap
    - (Posterior) predictive check
    - Sensitivity analysis
  8. Best practices and regulatory guidance
    - Data analysis plan
    - Data specification document
    - Audit trail and traceability
    - Software qualification
    - Relevant guidance documents
    - Population PK report
    - Use of population PK results in labeling
    - Overview of population modeling process
    - Exercise: create data analysis plan