

May 23-26, 2004: Buffalo, New York

PHARMACOKINETIC-PHARMACODYNAMIC MODELING

Concepts and Applications

COURSE OUTLINE

Over the past decade, significant progress has been made in the theory and applications of *pharmacodynamics*. On the basis of diverse *pharmacokinetic-pharmacodynamic modeling* concepts it has become possible to describe and predict the time course of drug effects under physiological and pathological conditions. The study of pharmacokinetic-pharmacodynamic relationships can be of considerable value in understanding drug action, summarizing extensive data, finding optimal dosing regimens, and in making predictions under new circumstances. Not surprisingly, pharmacokinetic-pharmacodynamic modeling concepts are increasingly applied in both basic research as well as in drug development.

This course will deal with the theoretical aspects and with the applications of pharmacokinetic and pharmacodynamic modeling. Subjects that will be discussed include:

Basic pharmacodynamic theory: receptor binding, post-receptor events, concentration-effect-time relationships.

Pharmacokinetic complexities: e.g. the role of distribution, metabolites, protein binding, the implications for the design of *in vivo* pharmacodynamic investigations; use of biomarkers and surrogate responses, models for pharmacogenomics;

Biophase compartment modeling: parametric, semi-parametric and non-parametric approaches;

Physiological pharmacodynamic modeling: indirect response models, cell lifespan models, chemotherapeutic effects;

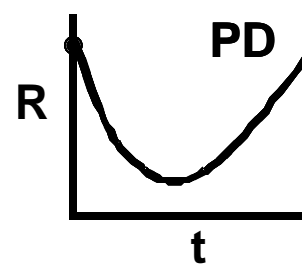
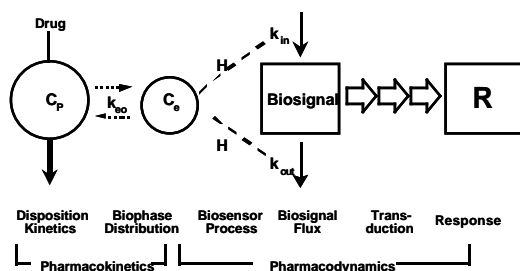
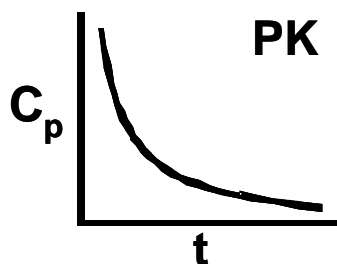
Pharmacodynamic drug-drug interactions: isobolograms, competitive and non-competitive interactions;

Functional tolerance development: desensitization, counter-regulation, physiological feedback, indirect precursor models;

Population pharmacodynamics: application of NONMEM in pharmacodynamics, issues in use of covariates.

Specific drug applications: CNS active agents, cardiovascular agents, corticosteroids, anticoagulants, antibodies, antibiotics.

Special topics: Signal transduction, circadian rhythms, target-mediated PK/PD models, disease progression models.



COURSE DIRECTION

William J. Jusko, PhD

Dr. Jusko is Professor and Chair of Pharmaceutical Sciences at the School of Pharmacy and Pharmaceutical Sciences at the University at Buffalo. Dr. Jusko supervises a research program on the pharmacokinetics and pharmacodynamics of immunosuppressive drugs such as corticosteroids, tacrolimus and sirolimus and holds three NIH grants in areas such as corticosteroid PK/PD, mathematical modeling, and biomedical computation. He has authored over 430 publications and consults for the FDA, NIH and the pharmaceutical industry.

Meindert Danhof, PhD

Dr. Danhof is Professor and Head, Division of Pharmacology at the Leiden/Amsterdam Center for Drug Research in the Netherlands. In that capacity he is Director of the multidisciplinary research program on "Mechanism-Based Pharmacokinetic and Pharmacodynamics Modeling of CNS Drug Effects" with additional interests in characterizing cardiovascular drugs. He has published 220 full publications in peer-reviewed international scientific journals, 24 book chapters and co-edited one book.

 **University at Buffalo**
The State University of New York at Buffalo
School of Pharmacy and Pharmaceutical Sciences

**Leiden/Amsterdam
Center for Drug Research**
Leiden University/Vrije Universiteit Amsterdam

COURSE PROGRAM

May 23 Sunday

6:00-7:00 Registration/Reception
7:00-8:00 Dr. W.J. Jusko: **History & Highlights**
8:00-9:30 Dinner

May 24 Monday

08:00 Continental Breakfast
08:30-08:45 Dr. W.J. Jusko: **Introductions**
08:45-09:45 Dr. W.J. Jusko: **Basic Pharmacologic Theory**
09:45-10:45 Dr. M. Danhof: **Kinetics of Pharmacologic Effects**
10:45-11:00 Coffee
11:00-12:00 Dr. M. Danhof: **Modeling Biophase Distribution**
12:00-01:00 Lunch
01:00-02:00 Dr. W.J. Jusko: **Basic Indirect Response Models**
02:00-03:00 Dr. W. J. Jusko: **Complexities of Indirect Responses**
03:00-03:30 Break
03:30-04:15 Dr. W. Krzyzanski: **Cell Lifespan Models**
04:15-05:00 Dr. M. Danhof: **Markers of Pharmacologic Action**

May 25 Tuesday

08:00 Continental Breakfast
08:30-09:45 Dr. M. Danhof: **Practical Exercises I**
09:45-10:00 Coffee

10:00-11:00 Dr. W.J. Jusko: **Modeling Irreversible Effects**
11:00-12:00 Dr. W.J. Jusko: **Modeling Functional Adaptation**
12:00-01:00 Lunch
01:00-02:00 Dr. H.L. Fung: **Cardiovascular Drug PK/PD**
02:00-03:00 Dr. M. Danhof: **Modeling Nonlinear Transduction**
03:00-03:15 Refreshments
03:15-04:15 Dr. W J Jusko: **Time-Dependent Transduction**
04:15-05:15 Dr. M. Danhof: **Modeling Drug Interactions**

May 26 Wednesday

08:00 Continental Breakfast
08:30-09:45 Dr. W.J. Jusko: **Practical Exercises II**
09:45-10:00 Coffee
10:00-11:00 Dr. J. Balthasar: **Monoclonal Antibodies**
11:00-12:00 Dr. D.E. Mager: **Target-Mediated PK/PD Models**
12:00-01:00 Lunch
01:00-02:00 Dr. W.J. Jusko: **Disease Progression Models**
02:00-03:00 Pf. J. Feidler-Kelly: **Population PK/PD Models**
03:00-03:15 Refreshments
03:15-04:15 Dr. W.J. Jusko: **Computational Issues in PK/PD**
04:15-04:30 Dr. W.J. Jusko: **Final Discussion and Summary**

REGISTRATION INFORMATION

Course location: The course will be held at the University Inn & Conference Center, 2401 N. Forest Road, Amherst, New York 14226-0823, U.S.A. Phone: (716) 636-7500. Fax: (716) 636-8296. The Conference Center is 15 min from Buffalo International Airport.

The price is \$ 66/day. **Hotel Deadline:** April 23, 2004.

Fee: Individual fee: \$1700. This includes course documentation, mid-session refreshments, lunches, and opening dinner during the course.

Up to 5 graduate students may enroll at a fee of \$850.

US Government rate: \$1400

Registration: Please register ASAP in view of the limited course capacity of 36 participants. Confirmation of registration will be returned upon receipt, together with an invoice for the course fee. Registration will not be final until payment is received.

Cancellations: Cancellations with a full refund may be made until March 31, 2004. No refund is possible on cancellations received after this date. Substitutions may be made at any time.

Ancillary Course: This course will be followed by an optional 2-day hands-on tutorial course in "Use of WinNonlin for PK/PD Modeling" with primary instruction by Dr. Jeffrey Wald from GSK. This course will utilize the Computer Laboratory at The University at Buffalo. An additional fee of \$900 is required. (Govt. \$700, Students \$450).

Payment: University at Buffalo Foundation Inc. Bank transfers and credit card payments are accepted as well as checks.

REGISTRATION FORM: Pharmacokinetic-Pharmacodynamic Modeling, May 23-26, 2004. WinNonlin, May 27-28, 2004.

Name _____ Title _____ Organization _____

Address _____

City _____ State/Country _____ Postal Code _____

Telephone _____ Fax _____

Email _____

Opening Reception/Dinner, Sunday, May 23, 6:00 PM: _____ Will Attend _____ Will Not Attend _____ Vegetarian Meal Requested _____

WinNonlin Course on PK/PD Modeling _____ Will Attend _____ Will Not Attend _____

Signature _____

Date _____

Please return to: PK/PD MODELING, Department of Pharmaceutics, School of Pharmacy, State University of NY at Buffalo, 519 Hochstetter Hall, Buffalo, NY 14260, Phone: 716 645 2842, ext. 224; Fax: 716 645 3693. Email: wjjusko@buffalo.edu.