

May 19- 22, 2002, Buffalo, New York 14260, U.S.A.

# PHARMACOKINETIC-PHARMACODYNAMIC MODELING

## Concepts and Applications

### COURSE OUTLINE

In recent years significant progress has been made in the area 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 drug development.

This course will deal with the theoretical aspects and with the applications of simultaneous pharmacokinetic/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, enantiomers, protein binding, the implications for the design of *in vivo* pharmacodynamic investigations;

**Effect compartment modeling:** parametric, semi-parametric and non-parametric approaches; biophase kinetics;

**Physiological pharmacokinetic-pharmacodynamic modeling:** e.g. indirect response models, chemotherapeutic effects;

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

**Functional tolerance development:** inhibitory metabolite models, physiological feedback models, indirect models;

**Population pharmacodynamics:** application of NONMEM in pharmacodynamics.

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

**Special topics:** Transduction, circadian rhythms, monoclonal antibodies, clinical trials simulation.

### COURSE DIRECTION

#### William J. Jusko, PhD

Dr. Jusko is Professor of Pharmaceutical Sciences at the School of Pharmacy and Pharmaceutical Sciences at the University of Buffalo, U.S.A. As Director of the Pharmacokinetics Laboratory, Dr. Jusko supervises a research program on the pharmacokinetics and pharmacodynamics of immunosuppressive drugs such as corticosteroids, tacrolimus and sirolimus. Over the past 30 years, his research interests have also involved clinical, basic, and theoretical aspects of diverse drugs such as cardiac agents, antibiotics, antidepressants, theophylline, as well as effects of tobacco smoking, oral contraceptives, obesity, and reversible metabolism. He has authored over 400 publications and consults for the FDA, NIH, and pharmaceutical industry.

#### Jaap W. Mandema, PhD

Dr. Mandema is currently Vice-President, Scientific Affairs, at Pharsight Corporation, Palo Alto, CA. He was previously at ALZA Corporation and Assistant Professor in the Department of Anesthesia, Stanford University School of Medicine. From 1987-1991 he was with the Center for Bio-Pharmaceutical Sciences, the Netherlands and from 1991-1992 with Dr. L.B. Sheiner at the University of California at San Francisco. Dr. Mandema has extensive experience with pharmacokinetic-pharmacodynamic modeling (in particular of CNS active, analgesic, and anesthetic drugs), population analysis (NONMEM), and clinical trials simulation.

#### Meindert Danhof, PhD

Dr. Danhof is Professor and Head, Division of Pharmacology at the Leiden/Amsterdam Center for Drug Research (LACDR), Leiden University, the Netherlands and Adjunct Professor of Pharmacetics, State University of New York at Buffalo. Dr. Danhof supervises research on pharmacokinetics and pharmacodynamics. His research projects include the pre-clinical and clinical pharmacodynamics of CNS active drugs (hypnotics, sedatives, anti-epileptics, opiates and anti-Parkinson drugs), cardiovascular drugs (calcium antagonists, adenosine receptor agonists and antagonists) and anticoagulants (heparinoids). He is editor of "The In Vivo Study of Drug Action-Concepts and Applications of Kinetic-Dynamic Modeling".

## COURSE PROGRAM

**May 19 Sunday**

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

**May 20 Monday**

08:00 Continental Breakfast  
 08:30-08:45 Dr. W.J. Jusko: **Introductions**  
 08:45-09:45 Dr. W.J. Jusko: **Basic Pharmacodynamic Theory**  
 09:45-10:45 Dr. M. Danhof: **Kinetics of Pharmacologic Effects**  
 10:45-11:00 Coffee  
 11:00-12:30 Dr. M. Danhof: **Modeling Reversible Drug Effects**  
 12:30-01:30 Lunch  
 01:30-03:30 Dr. W.J. Jusko: **Modeling Indirect Responses: Basic Concepts and Complexities**  
 03:30-04:00 Break  
 04:00-05:30 Dr. M. Danhof: **Measurement of Drug Action and Pharmacokinetic Complexities**

**May 21 Tuesday**

08:00 Continental Breakfast  
 08:30-10:00 Dr. M. Danhof: **Practical Exercises I**  
 10:00-10:15 Coffee  
 10:15-11:15 Dr. W.J. Jusko: **Modeling Irreversible Effects**

11:15-12:15 Dr. M. Danhof: **Modeling Functional Adaptation**  
 12:15-01:15 Lunch  
 01:15-02:00 Dr. W.J. Jusko: **Modeling Transduction Processes**  
 02:00-03:00 Dr. W. Krzyzanski: **Extended Indirect Response Models**  
 03:00-03:15 Refreshments  
 03:15-04:00 Dr. M. Danhof: **Preclinical PK/PD in Drug Development**  
 04:00-05:00 Dr. J.W. Mandema: **Modeling Drug Interactions**

**May 22 Wednesday**

08:00 Continental Breakfast  
 08:30-10:00 Dr. W.J. Jusko: **Practical Exercises II**  
 10:00-10:15 Coffee  
 10:15-12:00 Dr. J.W. Mandema: **Population Pharmacodynamics**  
 12:00-01:00 Lunch  
 01:00-02:30 Dr. J.W. Mandema: **Clinical Trials Simulation**  
 02:30-03:30 Dr. J. Balthasar: **Monoclonal Antibodies**  
 03:30-03:45 Refreshments  
 03:45-04:30 Dr. W.J. Jusko: **Some Computational Issues**  
 04:30-04:45 Dr. W.J. Jusko: Final Discussion

## 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 10 min from Buffalo International Airport. The price is \$ 66/day. **Hotel Deadline:** April 20, 2002.

**Fee:** Individual fee: \$1500.-. This includes course documentation, mid session refreshments, lunches and one dinner during the course.

Up to 5 graduate students may enroll at a fee of \$800.  
 US Government rate: \$1,200

**Registration:** Please register ASAP in view of the limited course capacity of 32 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 30, 2002. No refund is possible on cancellations received after this date. Substitutions may be made at any time. The organization reserves the right to cancel the course should the number of registrations be lower than 10. Notice of cancellation, with a full refund, will be given before April 30, 2002.

**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 staff from Pharsight Corp.. This course will utilize the Computer Laboratory at The University at Buffalo. An additional fee of \$800 is required. (Govt. \$600, Students \$400).

**Payment:** University at Buffalo Foundation Inc.

### REGISTRATION FORM: Pharmacokinetic-Pharmacodynamic Modeling, May 19-22, 2002. WinNonlin, May 23-24, 2002

Name \_\_\_\_\_ Title \_\_\_\_\_ Organization \_\_\_\_\_

Address \_\_\_\_\_  
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 \_\_\_\_\_

City \_\_\_\_\_ State/country \_\_\_\_\_ Postal Code \_\_\_\_\_

Telephone \_\_\_\_\_ Fax \_\_\_\_\_

Email \_\_\_\_\_

Opening Reception/Dinner, Sunday, May 19, 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 2855, ext. 224; Fax: 716 645 3693. Email: wjjusko@acsu.buffalo.edu.**