

# 2-DAY WORKSHOP ON MONOCLONAL ANTIBODY PHARMACOKINETICS & PHARMACODYNAMICS

## Concepts and Applications

### COURSE OUTLINE

This workshop has been designed to provide a detailed discussion of issues relevant to the pharmacokinetic / pharmacodynamic (PK/PD) modeling of antibody drugs. Lectures will address primary determinants of antibody pharmacokinetics (PK) and pharmacodynamics (PD), the design and implementation of pre-clinical investigations of antibody PK/PD, and state-of-the-art mathematical models to characterize and predict antibody PK and PD. Special emphasis is placed on discussion of the role of FcRn on the absorption, distribution, and elimination of antibodies, on the mathematical modeling of target-mediated antibody disposition, and on physiologically-based modeling of antibody pharmacokinetics. The workshop content is provided as a combination of formal lectures and informal review sessions.

Subjects that will be presented include:

**Determinants of antibody pharmacokinetics and pharmacodynamics:** mechanisms of antibody elimination, the role of convection in the kinetics of antibody distribution, the role of FcRn in antibody absorption, distribution, and elimination

**Common analytical assays for quantification of antibody in biological samples & implications for PK/PD investigations**  
**Immunogenicity and Antibody PK/PD**

**Evaluation of biosimilarity of antibody drugs:** Application of PK/PD for biosimilarity studies – opportunities and limitations

**Interspecies Scaling of Antibody PK**

**Target-Mediated Antibody Disposition:** modeling, implications for interspecies scaling, implications for First-in-Human studies

**Modeling of bimolecular antibody-ligand interaction**

**Physiologically-based pharmacokinetic modeling:** Incorporation of FcRn-mediated antibody transport in PBPK models, incorporation of target-mediated disposition, use of PBPK and preclinical data to predict antibody disposition in humans

### COURSE DIRECTION

**Joseph P. Balthasar, PhD.** Dr. Balthasar is Professor of Pharmaceutical Sciences and Director of the Center for Protein Therapeutics. His research interests include the development and preclinical evaluation of anti-toxin immunotherapies, the development and preclinical evaluation of anti-cancer immunotherapies (including immunoconjugate immunotherapies), and the development and preclinical evaluation of novel immunotherapies for humoral autoimmune conditions (immune thrombocytopenia, myasthenia gravis). He serves as a consultant to the NIH and pharmaceutical industry.

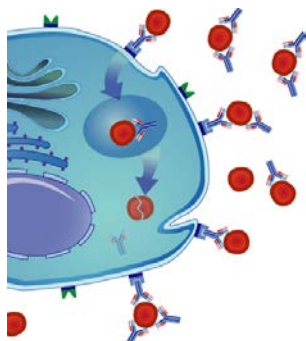
**Dhaval Shah, PhD.** Dr. Shah, Assistant Professor of Pharmaceutical Sciences, will provide lectures relating to the impact of anti-drug antibodies on mAb pharmacokinetics, and he will discuss mechanistic modeling of the PKPD of antibody-drug conjugates.



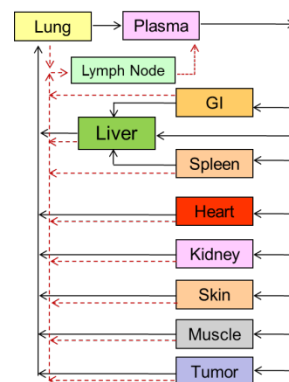
Joseph P. Balthasar, PhD



Dhaval Shah, PhD



University at Buffalo  
School of Pharmacy and  
Pharmaceutical Sciences



# AGENDA

## Day 1

8:15-8:45 **Continental Breakfast**  
 8:45-9:00 **Introductions**  
 9:00-11:00 **Introduction to Antibody Pharmacokinetics**

- Introduction to antibodies (isotypes, polyclonal vs. monoclonal, humanization, etc.)
- Mechanistic determinants of antibody absorption, distribution, and elimination (contrasting with determinants of small-molecule ADME)
- Comments on the mathematical modeling of antibody PK
- Recent research relating to the role of FcR and mAb PK

11:00-11:15 Break

11:15-11:40 **Analytical Assays for Antibodies: Implications for PK/PD Analyses**

- Discussion of major types of analytical assays for monoclonal antibodies (ELISA, RIA, LC MS/MS, SPR, “direct” labeling)
- Examples / case-studies

11:40-12:00 **Immunogenicity and Macromolecule PK/PD**

- Factors associated with immunogenicity
- Identification of host “anti-drug” antibodies
- PK modeling

12:00-1:00 Lunch

1:00-1:30 **Use of PK/PD Studies to Support Comparability Assessments of Therapeutic Proteins**

1:30-2:15 **Interspecies Scaling of Antibody PK & PD**

- General review of interspecies scaling
- Considerations for scaling antibody pharmacokinetics
- Examples / case-studies

2:15-3:30 **Mathematical Modeling of Target-Mediated Disposition of Monoclonal Antibodies**

- Introduction to TMD of Mab with examples
- Review of mathematical models that have been applied to characterize Mab TMD
- Comparison of model performance; discussion of implications for predicting Mab PK/PD

3:30-3:45 Break

3:45 - 4:15 **Biologics and Drug-Drug Interactions**

- Mechanisms
- Examples / case-studies

4:15-5:00

**Review Module #1: Design & Analysis of a Preclinical Investigation of Antibody PK**

- Study objectives
- Consideration for study design
- Assay considerations
- Initial evaluation of data (Additional studies needed?)
- Initial characterization of ADME (NCA vs. modeling)
- Evaluation of NCA results

6:00-7:30

**Group Dinner**

## Day 2

8:30-9:00

**Continental Breakfast**

9:00-10:00

**Mathematical Modeling of Bimolecular Antibody-Antigen Interaction**

- Review of binding kinetics (Law of Mass Action, equilibrium vs. non-equilibrium binding)
- Mathematical modeling of antibody binding: Examples from antibodies used for immunotoxotherapy

10:00-11:00

**Physiologically-Based PK Modeling of Mab**

- Review of PBPK models
- Application of PBPK models applied to Mab
- Discussion of major features of PBPK models for Mab & discussion of associated physiology (convection, restriction coefficients, sites of catabolism, “two-pore formalism”, incorporation of specific binding, incorporation of FcRn)

11:00-11:15

Break

11:15-12:00

**Review Module #2: Design & Analysis of a Preclinical Investigation of Antibody PK (Part 2)**

- Development of mechanistic mathematical models

12:00-1:00

Lunch

1:00-2:00

**Application of PK/PD Theory to Guide the Discovery and Development of New Immunotherapies**

2:00-2:30

**Review Module #3: Prediction of the Influence of Shed Antigen on the Distribution of Mab in Solid Tumors**

- Model development & simulations

2:30-2:45

Break

2:45-4:00

**Review Module #4**

- Discussion questions and review

# REGISTRATION DETAILS

**Course location:** The course will be held at The Conference 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>

**Hotel location:** *Sheraton at the Falls*, 300 Third St., Niagara Falls, NY 14303. USA. Phone: (716) 285-3361. The price is \$124/night single & double occupancy (add \$10 per person for triple & quadruple occupancy). *Hotel Deadline: April 3<sup>rd</sup>, 2017*. Website: <https://www.starwoodmeeting.com/Book/UBPharmacokinetic2016>

**Fee:** The fee is \$1800. A US government employee rate of \$1200 and student rate of \$800 is available for up to 3 participants of each type. The registration fee includes course documentation and handouts. Group dinner (Day 1), continental breakfasts, lunches and break-time refreshments during the course are included.

**Registration:** Online registration will begin October 15<sup>th</sup>, 2016. Given the special nature of the course, enrollment will be limited to 30 persons. Confirmation email of registration will be returned upon successful registration at the following website: <http://pharmacy.buffalo.edu/> under Quick Links.

**Cancellations:** Cancellations with a full refund may be made until March 13, 2017. No refund is possible on cancellations received after this date. Substitutions may be made at any time. Please inform course secretary of any substitutions.

**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](mailto:mis@buffalo.edu), if you need further assistance.