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

**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

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**COURSE DIRECTION**

**Joseph P. Balthasar, PhD**

Dr. Balthasar is Professor of Pharmaceutical Sciences at the University at Buffalo, State University of New York and Director of the Center for Protein Therapeutics. His PK/PD modeling interests and capabilities 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 the pharmaceutical industry.
### AGENDA

**January 13th, 2012**

<table>
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<tr>
<th>Time</th>
<th>Session</th>
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<tr>
<td>08:00</td>
<td>Continental breakfast</td>
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<tr>
<td>08:45-09:00</td>
<td><strong>Introductions</strong></td>
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<tr>
<td>09:00-10:45</td>
<td><strong>Introduction to Antibody Pharmacokinetics</strong></td>
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<td>10:45-11:00</td>
<td>Break</td>
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<tr>
<td>11:00-12:00</td>
<td><strong>Mathematical Modeling of Target-Mediated Disposition of Monoclonal Antibodies</strong></td>
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<td>12:00-13:00</td>
<td>Lunch</td>
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<td>13:00-14:00</td>
<td><strong>Mathematical Modeling of Bimolecular Antibody-Antigen Interaction</strong></td>
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<tr>
<td>14:00-14:30</td>
<td><strong>Interspecies Scaling of Antibody PK &amp; PD</strong></td>
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<td>14:30-14:45</td>
<td>Break</td>
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<tr>
<td>14:45-15:45</td>
<td><strong>Physiologically-Based PK Modeling of Mab</strong></td>
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<td>15:45-16:15</td>
<td><strong>Biologics and Drug-Drug Interactions</strong></td>
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<td>16:15-17:00</td>
<td><strong>Application of PK/PD Theory to Guide the Discovery and Development of New Immunotherapies</strong></td>
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### Course location: Faculté des Sciences Pharmaceutiques et Biologiques, Université de Paris Descartes, http://www.pharmacie.parisdescartes.fr/fc.

**Fee:** Individual fee: 900 euros before December 1, 2011, which includes course documentation, mid-session refreshments, and lunches (1000 euros after this date).

**Registration:** Please register ASAP in view of the limited course capacity. 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 December 14, 2011. No refund is possible on cancellations received after this date. Substitutions may be made at any time.

**Payment:** By check only for French public to l’Agent Comptable de l’université Paris Descartes or by bank transfer to:

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**Mathematical modeling of antibody binding:**

- Examples from antibodies used for immunotoxicotherapy

**Interspecies Scaling of Antibody PK & PD**

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

**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)

**Biologics and Drug-Drug Interactions**

- Biologics as DDI victims
- Biologics as DDI perpetrators
- Mechanisms / Examples

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

- Examples / discussion

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**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

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**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

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**Mechanisms / Examples**

- Review of binding kinetics (Law of Mass Action, equilibrium vs. non-equilibrium binding)
- Review of antibody PK
- Determinants of small-molecule ADME
- Antibody PK & immunotherapies
- Antigen interaction
- Recent research relating to the role of FcR and mAb PK

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**Application of PBPK models applied to Mab**

- Application of PBPK models 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)

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**Biologics as DDI victims**

- Biologics as DDI perpetrators
- Mechanisms / Examples

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

- Examples / discussion

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**Interspecies Scaling of Antibody PK & PD**

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

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**PBPK models**

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

- Examples / discussion