



## **Role of Pharmacokinetics in Establishing Bioequivalence for Orally Inhaled Drug Products**

Coordinated with Respiratory Drug Delivery (RDD) and the Product Quality Research Institute (PQRI)

### **Meeting Objectives**

*To evaluate the current state of knowledge and identify gaps in information for the potential application of pharmacokinetics (PK) as the sole indicator of in vivo bioequivalence of local delivery OIPs, addressing the power of the PK approach to detect differences in product performance in comparison with in-vitro and PD/clinical studies.*

**Thursday, April 29, 2010**

**International Ballroom**

- 8.30 a.m.     **Chairperson and Advocate:**  
*Dennis O'Connor, B.S., Boehringer Ingelheim, Ridgefield, CT*
- 8.45 a.m.     Evolution of Regulatory and Scientific Paradigms for Establishing Equivalence of Systemic Exposure from Orally Inhaled Drugs: Current Status and Possible Challenges  
*Gur Jai Pal Singh, Ph.D., Scientific Advisor, Corona, CA*
- 9.15 a.m.     Demonstrating Bioequivalence using Pharmacokinetics: Theoretical Considerations across Drug Classes.  
*Guenther Hochhaus, Ph.D., University of Florida, Gainesville, FL*
- 9.45 a.m.     The Clinical Utility of Pharmacokinetics in Demonstrating Bioequivalence of Locally Acting OIPs.  
*Peter T. Daley-Yates, Ph.D., GlaxoSmithKline, Uxbridge, United Kingdom*
- 10.15 a.m.    **Refreshments**
- 10.45 a.m.    Aspects of Pharmacokinetic Study Design to Differentiate Between Different Orally Inhaled Drug Products  
*Lars Borgstrom, Ph.D., AstraZeneca, Lund, Sweden*

11.15 a.m. Application of the EU Guidelines for Pharmacokinetic Studies of Locally Acting Orally Inhaled Drug Products  
*Sanjeeva Dissanayake, M.R.C.P., Medicines and Healthcare Products Regulatory Agency (MHRA), London, United Kingdom*

11.45 a.m. Panel Discussion

**Panel:**

Lars Borgstrom, Ph.D., AstraZeneca  
Badrul A. Chowdhury, M.D. Ph.D., U.S. Food and Drug Administration  
Dale Conner, Ph.D., U.S. Food and Drug Administration  
Peter T. Daley-Yates, Ph.D., GlaxoSmithKline  
Sanjeeva Dissanayake, M.R.C.P., MHRA  
Gunther Hochhaus, Ph.D., University of Florida  
Gur Jai Pal Singh, Ph.D., Scientific Advisor

**12.15 p.m. Luncheon**

**Friday, April 30, 2010**

*National Ballroom D*

Moderator Myra Herrle, Ph.D., R.Ph.  
Novartis Pharmaceuticals

8.30 a.m. **Salmeterol/Fluticasone propionate Diskus® versus Salmeterol/Fluticasone propionate RPID®**  
Peter Daley-Yates, Ph.D.  
GlaxoSmithKline

8.55 a.m. **Formoterol Certihaler™ versus Formoterol Aerolizer®**  
Beverley E. Patterson, Ph.D.  
Novartis Pharmaceuticals

9.20 a.m. **Salbutamol (INN) MDI versus Salbutamol Originator MDI**  
Anders Fuglsang, Ph.D.  
Aeropharm GmbH

9.45 a.m. **Panel Discussion**

10.00 a.m. **Refreshments**

10.30 a.m. **Breakout Sessions**  
Meeting participants may select and attend one of the following Breakout Sessions

**Session 1: PK and Lung Deposition**

*Wentworth*

Facilitators: Steve Newman, Ph.D., Scientific Consultant  
Gunther Hochhaus, Ph.D., University of Florida  
Sau Lee, Ph.D., Food and Drug Administration

*Potential discussion points:*

- a. *What is the relationship between PK data and drug deposition?*
- b. *Can radionuclide imaging studies support PK methods for assessing BE? What are the design criteria for these imaging studies?*
- c. *Is the "C/P ratio" enough to assess regional lung deposition?*
- d. *Are there PD data that correlate with regional lung deposition data?*
- e. *Can PK methods establish the equivalence of regional lung deposition?*

**Session 2: PK and *In Vitro* Assessment                      *Augusta***

Facilitators: Martin Oliver, R.Ph., Vectura Limited  
Guirag Poochikian, Ph.D., Scientific Consultant  
Wallace Adams, Ph.D., R.Ph., Food and Drug Administration

*Potential discussion points:*

- a. *Does it matter if there is an agreement between PK and in vitro data?*
- b. *Using in vitro data to assess the sensitivity of PK methods.*
- c. *What are the sources of variance in in vitro measurements? How does this variance affect the interpretation of PK data?*
- d. *Can in vitro measurements predict the C/P ratio?*
- e. *What criteria or attributes were most supportive in demonstrating BE for the case studies (presented Friday morning)?*
- f. *Stepwise approach: what are the requirements to accept in vitro and PK data?*

**Session 3: PK and PD Relationships                      *Congressional B***

Facilitators: Murray Ducharme, Pharm.D., Cetero Research  
Hartmut Derendorf, Ph.D., University of Florida  
Sandra Suarez-Sharp, Ph.D., Food and Drug Administration

*Potential discussion points:*

- a. *Links between PK and PD data.*
- b. *Charcoal block for drugs with different bioavailability (oral vs lung).*
- c. *Demonstration of lung-specific absorption.*
- d. *Assessment of power requirements in clinical studies.*
- e. *What criteria or attributes were most supportive in demonstrating BE for the case studies (presented Friday morning)?*

**Session 4: Effective PK Study Designs                      *Royal Dublin B***

Facilitators: Tushar Shah, M.D., Teva Pharmaceuticals  
John Davis, Ph.D., Pfizer  
Partha Roy, Ph.D. / Bing Li, Ph.D, Food and Drug Administration

*Potential discussion points:*

- a. *Differences in:*
  - i. *healthy subjects vs patients,*
  - ii. *asthma, COPD, cystic fibrosis; disease severity*
  - iii. *pediatric*
  - iv. *geriatric*
- b. *Will the people/technique variability limit the applicability/usefulness of PK studies?*
- c. *PK population approaches*
- d. *Training of patients in PK studies.*
- e. *Contribution of various sources of variability to the reliability of PK studies.*

12.00 noon    **Lunch**

1.00 p.m.    **Breakout Sessions**

Breakout sessions will be repeated including feedback from the first session. Meeting participants may select and attend one of the following:

**Repeat of Session 1:**

PK and Lung Deposition

**Repeat of Session 2:**

PK and *In Vitro* Assessment

**Repeat of Session 3:**

PK and PD Relationships

**Repeat of Session 4:**

Effective PK Study Designs

2.30 p.m.    **Refreshments**

3.30 p.m.    **Review of Breakout Sessions**

4.30 p.m.    **Panel Discussion**

5.00 p.m.    **Closing Remarks**