From the Creators of Drug Formulation & Bioavailability:

BIOEQUIVALENCE
SUMMIT

September 15-16, 2014
Hyatt Regency Cambridge
Cambridge, MA

Sharing Best Practice to Meet Regulatory Expectations and Demonstrate Bioequivalence for Challenging Drug Formulation and Delivery Methods

FEATURED SPEAKERS

AUDRA STINCHCOMB
CSO
ALLTRANZ

GARY BUEHLER
VP, Regulatory Strategic Operations
TEVA

ROBERT BAUGHMAN
Senior VP, Clinical Sciences
MANNKIND CORPORATION

HENRY WU
Director, Biopharmaceutics
MERCK

SHEFALI KAKAR
Senior Director, Clinical Pharmacology
NOVARTIS

Streamline and Improve your Bioequivalence Test Designs and Regulatory Compliance!

TAKEDA Uses PK/PD Modeling to Establish IVIVC

DR. REDDY’S Hits Test Targets on Drugs with Narrow Therapeutic Indices

MERCK Compensates for the Variability of Food Activity on Drug Effects

Demonstrate Bioequivalence for Complex Formulations and Delivery Methods!

NOVARTIS Optimizes Test Parameters for Biosimilars

MANNKIND CORPORATION Secures Regulatory Approval for an Inhaled Formulation with Companion Device

BRISTOL-MYERS SQUIBB Addresses Compounds with Minimal or No Absorption in the GI Tract

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Co-located Event – Enhance your Networking Opportunities!

TECHNOLOGY TRANSFER FOR BIOLOGICS

Pion
Dear Colleague,

The biopharma industry is leaning on its formulation and PK/PD teams harder than ever before, in the hopes of being able to develop new compounds, brand extensions, and delivery methods that safeguard revenue from the patent cliff. And while it has never been more important that you be able to demonstrate that your new formulations are just as safe and effective as the originators, it has also never been more difficult: Regulatory guidelines lack harmonization across multiple countries and markets, and the development of new types of molecules and delivery methods has led to more difficulty in designing bioequivalence tests and more subjectivity in the interpretation of results.

I invite you to attend ExL Pharma’s Bioequivalence Summit – the conference offering the most up-to-date and comprehensive solutions to regulatory and technical challenges that you face while working to expand your product life cycle.

Only at this event will you find:

- Up-to-date insights on **global bioequivalence regulatory criteria**
- Exclusive case studies for the proper test designs for drugs with local sites of action, such as those with topical or inhalant delivery systems
- Best practice when in-vitro / in-vivo correlation is weak or absent
- Key strategies for proving bioequivalence in the first wave of biosimilar candidates in the U.S.

We look forward to welcoming you to Cambridge this Fall!

Sincerely,

Matt Greenbaum

Matt Greenbaum
Senior Conference Producer, ExL Pharma
mgreenbaum@exlpharma.com

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**HOTEL INFORMATION**

**Hyatt Regency Cambridge**
575 Memorial Drive
Cambridge, MA 02139

Room Reservation Information: To make reservations guests can call 1-888-421-1442 and request the negotiated rate for ExL Pharma’s September Meetings. The group rate is available until August 25th, 2014. Please book your room early as rooms available at this rate are limited.

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**WHO SHOULD ATTEND:**

- Bioequivalence
- Pharmacokinetics / Pharmacodynamics / PKPD / PKDM / DMPK
- Pharmaceutics / Biopharmaceutics
- Biostatistics
- Preclinical Research
- Formulation
- Preformulation
- Scientific Affairs
- Regulatory Affairs
- Drug Delivery
- Drug Discovery
- Life Cycle Management

**THIS CONFERENCE WILL ALSO BE OF INTEREST TO:**

- CROs
- CMOs
- Central Labs
- Regulatory Consultants
- Statistical Service Providers
- API Suppliers

**INTERESTED IN SPONSORSHIP & EXHIBITION OPPORTUNITIES?**

Do you want to spread the word about your organization’s solutions and services to potential clients who will be attending this event? Take advantage of the opportunity to exhibit, underwrite an educational session, host a networking event, or distribute promotional items to attendees. ExL Pharma will work closely with you to customize a package that will suit all of your needs. To learn more about these opportunities, please contact:

Jeffrey Friedman, Business Development Manager,
917-258-5163, jfriedman@exlpharma.com

**CO-LOCATED EVENT:**

Your registration at this event also allows you to network with the industry leaders taking part in ExL Pharma’s Technology Transfer for Biologics conference. To find out more about the topics and experts featured there, please see: [www.exlpharma.com/techtransfer](http://www.exlpharma.com/techtransfer)
9:00  Adapting your Testing Methods for NTI Drugs with High Dosage Units
Regulatory compliance can be especially challenging with drugs that are classified as having a Narrow Therapeutic Index and at the same time can only have their effective doses changed by large amounts. The risk of exceeding the confidence interval is very high, and preventing this requires more expensive tests than your company may be able to withstand. And will they be accepted in every market?
- Minimize variability to make it easier to hit AUC and CMAX targets
- Gauge the risks of redundant testing if different countries reach different conclusions about your drug’s NTI status
- Learn from the test result preferences of both U.S. and European agencies

Chandra Vattikonda, Senior Director, North America Generics, DR. REDDY’S LABORATORIES

9:45  CASE STUDY: Non-Clinical Tools for Performance Testing of Complex Drug Products
Karen Doucette, Associate Director, Operations, ABSORPTION SYSTEMS

10:30  Networking Refreshment Break

11:00  Complication of Food in Bioequivalence Testing: Regulatory Requirements and Design Implications
Depending on the drug and dosage form design, tests involving the food effect can significantly complicate your bioequivalence work and its outcome. The lack of harmonization on the relevant regulatory requirements presents major challenges for rapid and cost-effective global commercialization of new drugs.
- Understand the effect of food intake on pharmacokinetics of different classes of drugs and dosage forms
- Establish clinical strategy based on the current regulatory requirements for fasted vs fed bioequivalence studies
- Call for the need of harmonization on bioequivalence testing involving food

Henry Wu, Director, Biopharmaceutics, MERCK

11:45  CASE STUDY: In-Vivo Modeling and Simulation (IVMS) Approach for Establishing Bioequivalence
This presentation introduces the latest advanced approach to establish the bioequivalence for formulations by using In Vivo Modeling and Simulation (IVMS) in conjunction with in-vitro biorelevant dissolution experiments.
- Introduction of IVMS in drug development
- Biorelevant dissolution and drug release testings
- Bioequivalence projection, evaluation, and validation

Jeffery Liu, Principal Clinical Investigator, Medical Affairs, GLAXOSMITHKLINE

12:30  Luncheon

1:30  Sample Size Adaptive Sequential Design for Bioequivalence Studies with Crossover Designs: An Optimized Approach
Two papers present several solutions to the design problem for crossover studies, namely adaptive two-stage designs, allowing for re-estimation of the second-stage sample size based on first-stage results. These designs present and validate (in terms of preserving the type I error rate) what is possible with two-stage designs. However, there has not yet been an attempt to optimize their performance.
- Use adaptive two-stage designs for two-period crossover studies during optimal design spaces
- Introduce an upper limit for overall study size
- Analyze a futility criterion, which allows for the abandonment of a study after the first stage if there would be little hope of meeting BE criteria if the second stage were to be conducted

Diane Potvin, President, EXCELSUS STATISTICS

2:15  Biorelevant Approaches to In-Vitro Characterization
Magali Hickey, Director, Formulation Development, ALKERMES

3:00  Networking Refreshment Break

3:30  Novel PK/PD Modeling Approaches to Establishing IVIVC
Traditional techniques of comparing multiple release rates and formulations to establish bioequivalence have proven to be both difficult and expensive, at a time when the industry is under unprecedented pressure to do more with less. More advanced in-silico modeling techniques can be better methods for simulating plasma concentrations and thus establishing predictive models for new compounds.
- Fine-tune models of in-vitro dissolution rates to predict AUC and CMAX
- Run clinical trials around multiple simulations with a random set of parameters to find the strongest possible IVIVC
- Use modeling and prediction as bridging methods to lower testing burden

Arijit Chakravarty, Director, Modeling & Simulation (DMPK), TAKEDA

4:15  CASE STUDY: Determining when to use In-Vitro Characterization versus Comparative Clinical Trials during Oncology Drug Development
Evaluating the impact of a formulaulation or process change during development and prior to late stage development is critical in order to determine if the safety and effectiveness of the clinical trial material is impacted. Recent Draft FDA guidance (March 2014) provides general considerations for bioavailability and bioequivalence studies submitted in NDAs and INDs. For immediate-release formulations, options exist to provide in vitro data to demonstrate BA or BE in context of formulation changes. Conducting in-vitro characterization rather than clinical trials has many advantages in the oncology setting where clinical studies must involve dosing patients. This case study discusses various formulation changes for an immediate release drug product and the strategy behind recommending in-vitro characterization versus comparative clinical trials. It presents specialized analytical techniques for demonstrating material comparability of a unique formulation.
- Demonstrate how to apply draft FDA guidance to evaluate BA and BE for formulation changes during development
- Set strategies for implementing formulation changes during development
- Present specialized analytical characterization techniques and considerations for unique formulations

Elizabeth Hewitt, Senior Scientist, Analytical Development, Small Molecules, TAKEDA

5:00  End of Day One

TO REGISTER  Call 866-207-6528 or visit www.exlpharma.com/bioequivalence
TUESDAY, SEPTEMBER 16TH, 2014 / MAIN CONFERENCE, DAY TWO

8:00 Continental Breakfast

8:45 Recap of Day One from Chairperson

9:00 KEYNOTE: CASE STUDY – Inhalation Drug Delivery for Systemic Exposure – MannKind’s Experience with Inhaled Insulin

Elements of the drug device combination product, the orally inhaled dry powder delivery mode and various intrinsic factors created complexity in describing systemic insulin availability. In addition, the use of a novel excipient that is absorbed into the systemic circulation added a dimension not seen with other, locally acting, orally inhaled dry powder products. This session discusses traditional and innovative methodologies used in multiple PK/PD and long term studies, in the following contexts:

- Bioavailability of an endogenous substance
- Mass balance and relative bioavailability to other delivery modes
- Assessment of device influence on bioavailability/bioequivalence, including in-vitro assessment of intrinsic delivery factors
- Device bridging within the clinical setting

Robert Baughman, Senior VP, Clinical Sciences, MANNKIND CORPORATION

9:45 Approaches for Inhaled and Suspension Formulations that Avoid In-Vivo Bioequivalence

Locally-active formulations are a challenge that FDA regulators have examined at length. If generic formulations are qualitatively and quantitatively the same as the brand, FDA has traditionally decided to waive the requirement to demonstrate bioequivalence.

- Differentiate between test expectations for suspensions and solutions
- Prepare for comparative evaluation of metered inhalation device performance, safety, and PK
- Map the tests that will have the broadest applicability to an increasingly popular inhalation formulation within the generics industry

Guenther Hochhaus, Professor, Pharmaceutics, UNIVERSITY OF FLORIDA COLLEGE OF PHARMACY

10:30 Networking Refreshment Break

11:00 Feedback Loops between Patient Health and Drug Performance

Traditional drug R&D focused around healthy volunteers as a means of controlling as many factors as possible. But with more advanced molecules such as biologics, the protein level can itself be substantially influenced and manipulated by the well-being of the test subject. When it is best to use patients with drug-specific ailments as test subjects to prove the equivalence of formulation and delivery?

- Recognize thresholds of circulating receptor and ligand in body that will trap proteins and impact drug levels
- Predict which drugs are likely to be less bioequivalent in sick test subjects based on solubility and permeability
- Factor for physiological feedback between oral, kidney, and cardiac diseases and drug absorption

Raimar Loebenberg, Chair, Division of Pharmaceutical Sciences, UNIVERSITY OF ALBERTA

11:45 SPOTLIGHT: Drugs that are Unabsorbed in Local Activity in the GI Tract

Disease indications such as Crohn’s disease and ulcerative colitis are treated by therapeutics that have the GI tract as their local site of action. As these medicines heal intestinal erosions, they often stay within the GI tract without large-scale absorption. Monitoring drug levels and effects thus can radically depart from the typical absorption / PK-centered tests, requiring an entirely different approach.

- Distinguish between clinical trials that show overall drug effectiveness and those clearly showing equivalence between multiple formulations
- Set up dissolution tests at multiple pH levels to simulate drug levels throughout the GI tract
- Avoid the risks of overreliance on subtracting known absorbed drug levels

Gary Buehler, VP, Regulatory Strategic Operations, TEVA

John Crison, Research Fellow, BRISTOL-MYERS SQUIBB

12:30 Luncheon

1:30 CASE STUDY: Biopharmaceutical Considerations, IVIVC, and Heat Effects in the Development of Generic Transdermal Delivery Systems

Audra Stinchcomb, CSO, ALLTRANZ

2:15 Unique Study Considerations for Intraoral Dosage Forms

Protocol design and documentation requirements for bioequivalence testing of intraoral dosage forms such as orally dissolving tablets (ODT) and films (ODF) as well as sublingual/buccal tablets have significantly evolved in the last few years. By staying up to date with these expectations, you can not only improve your developability of these novel formulations but also carry forward valuable lessons from these tests into other dosage forms or delivery systems as well.

- Compare bioequivalence with and without water, both for new formulations and when comparing modifications and generics to existing formulations
- Determine the need for assessing intraoral absorption contribution
- Overlay your bioequivalence test designs with patient-centric data gathering

Henry Wu, Director, Biopharmaceutics, MERCK

3:00 Determining a Hierarchy of Parameters in Tests for Biosimilars

Since most biologics are administered directly to the bloodstream, their bioavailability is 100% and thus detecting their blood concentration is not necessarily a meaningful metric. If you cannot always rely on PK parameters, you must create a hierarchy of other means of determining biosimilar performance, and be prepared to perform multiple tests based upon differing sensitivity.

- Visualize multiple compositions of PD markers you could explore to demonstrate pharmacological equivalence
- Rank all possible PK and PD endpoints before undertaking the risk and expenses of new clinical trials
- Find creative solutions to gaps in the biosimilar regulatory approval guidelines

Shefali Kakar, Senior Director, Clinical Pharmacology, NOVARTIS

3:45 End of Conference

PRAISE FOR EXL PHARMA CONFERENCES ON DRUG FORMULATION AND BIOAVAILABILITY:

“An excellent event with very focused views of new technologies.”
– Senior CMC Team Leader, ALCON

“Informative and thought-provoking. Great discussions!”
– President, AMYLYX PHARMACEUTICALS

“Very good examples provided. Great explanations to questions raised!”
– Associate Director, Pharmaceutical Sciences, TAKEDA
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We offer a 30% registration discount for Academic / Non-Profit audience members. Please call 866-207-6528 for details.

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Questions? Comments?
Do you have a question or comments that you would like to be addressed at this event? Would you like to get involved as a speaker or discussion leader? Please email Program Director, Matt Greenbaum, at mgreenbaum@exlpharma.com

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☐ Yes! Register me for the Conference

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