


## AT A GLANCE

Monday	Tuesday	Wednesday	Thursday
		<p><b>8:30 am – 11:00 am</b> WEDNESDAY MORNING SYMPOSIA FUNDED BY A GRANT FROM</p> <p><b>AstraZeneca</b>  life inspiring ideas</p> <p><b>SYMPOSIUM</b> The Influence of Excipient Functionality on Quality by Design for Drug Product</p>	
	<p><b>9:00 am – 11:00 am</b> <b>ROUNDTABLES</b> Impact of Changing Regulations on Post-approval CMC Changes: U.S. and E.U. Perspectives</p> <p>How to Face and Successfully Defend FDA and Other Regulatory Audits</p>		
<p><b>2:00 pm – 4:00 pm</b> <b>ROUNDTABLE</b> Navigating the New Rules Regarding Patent Law: Decodifying ‘Obviousness’, ‘Limited Claims’, and How it Affects New Composition of Matter Patents</p>	<p><b>2:00 pm – 4:00 pm</b> TUESDAY AFTERNOON ROUNDTABLES FUNDED BY A GRANT FROM</p> <p><b>Catalent</b> </p> <p><b>ROUNDTABLES</b> Stability Evaluations Using Alternate Accelerated Conditions</p> <p>Bioequivalence Requirements: Challenges in Global Drug Development and Harmonization</p>	<p><b>2:00 pm – 4:00 pm</b> <b>ROUNDTABLE</b> Comparator Products – Untold Stories</p> <p><b>2:00 pm – 4:30 pm</b> WEDNESDAY AFTERNOON SYMPOSIA FUNDED BY A GRANT FROM</p> <p><b>sanofi aventis</b> Because health matters</p> <p><b>SYMPOSIA</b> Using the Quality-by-Design Principle to Establish Pharmaceutical Equivalence and Bioequivalence of Advanced Dosage Forms</p> <p>Microdialysis Role in the Development and Optimization of Drug Topical Delivery</p>	<p><b>1:30 pm – 5:00 pm</b> <b>OPEN FORUMS</b> Global Regulatory Challenges for Genotoxic Impurities</p> <p><i>An additional fee is required to attend this open forum</i></p> <p>Biosimilars- Development Considerations and Future Directions (BIOTEC &amp; RS)</p> <p><i>An additional fee is required to attend this open forum</i></p>
<p><b>2:00 pm – 4:30 pm</b> MONDAY AFTERNOON SYMPOSIA FUNDED BY A GRANT FROM</p> <p><b>Catalent</b> </p> <p><b>SYMPOSIUM</b> Regulatory Significance of Critical Quality Attributes and Critical Process Parameters in Successful Product Development and Commercialization</p>			
<p><b>5:30 pm – 7:30 pm</b> Regulatory Sciences (RS) Section Joint Membership Meeting and Reception</p>			

# AAPS Regulatory Sciences (RS) Programming

## New INTERACTIVE FEATURE for all Roundtable Sessions!

Click on roundtable moderator names to submit questions that you would like to be addressed at the roundtable session in Los Angeles.

### Monday, November 9, 2009

#### MONDAY AFTERNOON ROUNDTABLES

2:00 pm - 4:00 pm

#### Navigating the New Rules Regarding Patent Law: Decodifying 'Obviousness', 'Limited Claims', and How it Affects New Composition of Matter Patents

##### Roundtable

There have been continuous changes implemented by the US PTO to streamline the patent filing and approval process, and reduce patent prosecution times. With it have come several changes to the content of patents and continuation filings, which significantly impact/limit patenting chemical, pharmaceutical and biotech inventions. For example, U.S. and international law denies patentability to subject matter which is "obvious" or which lacks an "inventive step". However, such rulings differ from country to country. This roundtable will invite discussion from patent law experts regarding these recent developments, such as what counts as "obvious" in the context of chemical, pharmaceutical, and biotechnological inventions, limits on claims and continuation applications.

##### MODERATORS

Michael Bornstein, Ph.D.  
Bornstein Consulting, LLC

Jeffrey A. Lindeman, Ph.D.  
O'Brien Jones PLLC

#### New Regulations in Patent Law for the Pharma Industry

Scott Bornstein, J.D.  
Greenberg Traurig, LLC

##### Presentation Title to Be Determined

Barry Schindler, J.D.  
Greenberg Traurig, LLP

#### A Look at Post-KSR Cases: Is the Perceived Change Really that Great?

Irem (Remy) Yucel, Ph.D.  
U.S. Patent and Trademark Office

#### MONDAY AFTERNOON SYMPOSIA

FUNDED BY A GRANT FROM



2:00 pm - 4:30 pm

#### Regulatory Significance of Critical Quality Attributes and Critical Process Parameters in Successful Product Development and Commercialization

##### Symposium

Identification of the right critical quality attributes (CQA) of pharmaceutical materials and critical process parameters (CPP) of various manufacturing steps is extremely important for defining the design-space for a given pharmaceutical product. Defining an appropriate design space offers operational flexibility within the defined design-space and thus regulatory flexibility. However, given the multitude of quality attributes and process parameters, this can be a very complicated and time consuming exercise. The objective of this symposium is to provide case studies on how to establish the CQAs and CPPs for drug substance and various dosage forms.

##### MODERATORS

Lawrence X. Yu, Ph.D.  
U.S. Food and Drug Administration

Prabu Nambiar, Ph.D., M.B.A.  
Vertex Pharmaceuticals, Inc.

#### Introduction — Regulatory Significance of CQAs and CPPs

Prabu Nambiar, Ph.D., M.B.A.  
Vertex Pharmaceuticals, Inc.

#### CQA and CPP — FDA Perspectives

Elaine Morefield, Ph.D., invited  
U.S. Food and Drug Administration

#### CQAs and CPPs for Drug Substance

Stephen Colgan, Ph.D., invited  
Pfizer Global Research & Development

#### CQA and CPP for Immediate & Modified Release Dosage Forms

Shailesh Singh, Ph.D.  
Wyeth

#### JOINT MEMBERSHIP MEETING AND RECEPTION

5:30 pm - 7:30 pm

#### Regulatory Sciences (RS) Section Joint Membership Meeting and Reception

### Tuesday, November 10, 2009

#### TUESDAY MORNING ROUNDTABLES

9:00 am - 11:00 am

#### Impact of Changing Regulations on Post-approval CMC Changes: U.S. and E.U. Perspectives

##### Roundtable

An open discussion with regulators from North America and Europe with counterparts from industry. The focus will be on variations and changes when the process space has been defined by QbD methodology.

##### MODERATOR

Abbie Gentry, Ph.D.  
McNeil Consumer Healthcare

#### Strategies to Meet International Change Control Requirements by a U.S. Company

Thirunellai Venkateshwaran, Ph.D.  
Wyeth

9:00 am - 11:00 am

#### How to Face and Successfully Defend FDA and Other Regulatory Audits

##### Roundtable

In this session, we will share the experiences of U.S. Food and Drug Administration (FDA) officers, and clients' experience on how to face FDA scientific compliance or routine audits. This discussion will provide an insight on how to manage a crisis into a less painful and manageable exercise.

##### MODERATORS

Prasad N.V. Tata, Ph.D., F.C.P.  
Covidien/Mallinckrodt, Inc.

Raja Velagapudi, Ph.D.  
Barr Laboratories

#### Audits Have a Purpose — Understand Them and Comply with Them

C.T. Vishwanathan, Ph.D.  
U.S. Food and Drug Administration

#### We had an Audit, No Citation, No 483 Good News

Chinna Pammidi, Ph.D.  
Cetero Research

#### My CRO is Under Audit — What Should I Do?

Prasad N.V. Tata, Ph.D., F.C.P.  
Covidien/Mallinckrodt, Inc.

# AAPS Regulatory Sciences (RS) Programming

## TUESDAY AFTERNOON ROUNDTABLES

FUNDED BY A GRANT FROM



2:00 pm – 4:00 pm

### Stability Evaluations Using Alternate Accelerated Conditions

#### Roundtable

In the current environment, clinical materials are manufactured, packaged, tested, and distributed worldwide. During transition, there are inherent changes of degradation, physical stability, dissolution rate, and particle size that may be affected; thus increasing risk to clinical materials. This session will explore options to effectively maximize the data collected using predictive stability tools to support establishment of shelf-life for clinical materials and minimize the number of stability studies to support clinical program. This roundtable will discuss the use of alternate accelerated/stress conditions, scientific understanding and predictive stability tools as an aid in the development to reduce risk and increase extrapolation robustness while maintaining product safety. Challenges to establish alternative accelerated conditions for unusual dosage forms and implication of physical and chemical changes on formulation/packaging and shipping strategies. Studies supporting shipment of clinical and commercial product, including controlling the shipment, monitoring and justifying excursions that may be observed.

#### MODERATORS

Kim Huynh-Ba, M.S.  
PHARMALYTIK

Andrea Panaggio, Ph.D., M.S., R.Ph.  
Bristol-Myers Squibb

### Utilizing Stability and Analytical Tools to Improve Product Knowledge to Facilitate Support of a Global Clinical Program

Frank Diana, Ph.D.  
Endo Pharmaceuticals

### Formulation Development Study Strategies to Support Controlled Temperature Shipping

Sailesh A. Varia, Ph.D.  
Bristol-Myers Squibb

### Stability Conditions for Product Development Evaluations Pre-IND to Assure Acceptable Product During Shipment and Storage

Edward Koch  
McNeil Consumer Healthcare

2:00 pm – 4:00 pm

### Bioequivalence Requirements: Challenges in Global Drug Development and Harmonization

#### Roundtable

The pharmaceutical drug industry has become increasingly global. Bioequivalence and interchangeability requirements for registration of multisource (generic) pharmaceutical products vary in each domestic market place. Harmonization of these requirements would decrease duplication of studies and unnecessary human drug exposure. This symposium will bring together pharmaceutical scientists from industry and regulatory agencies to review scientific and regulatory issues that would begin a process of harmonization of bioequivalence requirements. Some issues to be discussed will include the selection of a reference listed drug product; the design of bioequivalence studies both *in vivo* and *in vitro* approaches; and the acceptance criteria for bioequivalence.

#### MODERATORS

Leon Shargel, Ph.D.  
Applied Biopharmaceutics

Raja Velagapudi, Ph.D.  
Barr Pharmaceuticals, Inc.

### International Bioequivalence Requirements

Gordon Johnston, M.S.  
Generic Pharmaceutical Association

### International Reference Listed Drug Product

Leon Shargel, Ph.D.  
Applied Biopharmaceutics

### Harmonization of Bioequivalence Requirements

Paul Fackler, Ph.D.  
Teva Pharmaceuticals

Wednesday, November 11, 2009

## WEDNESDAY MORNING SYMPOSIA

FUNDED BY A GRANT FROM



8:30 am – 11:00 am

### The Influence of Excipient Functionality on Quality by Design for Drug Product

#### Symposium

Excipients facilitate manufacturing, enhance or support stability, and/or aid *in vivo* performance of a product. Certificates of analysis provide little information about what the industry has termed excipient functionality. This demands thorough understanding of material characteristics such as particle size and morphology, solid-state characterization and processing to name a few. Functionality has become a hot topic since the European Pharmacopoeia (EP) listed specific functionality-related characteristics (FRCs) in some of its excipient monographs. USP has looked into including a General Chapter on Excipient Performance Testing suggesting it could be part of the labeling section and non-mandatory. Excipient manufacturers are voicing concerns because in their view functionality may mean different things to different people. The characterization of functionality is very simply process understanding in accordance with the philosophy of the U.S. Food and Drug Administration (FDA), PAT and 21st century GMP initiatives. QbD is an approach to product development that seeks to find the limits within which acceptable product can be manufactured (edge of failure) and thereby the approvable design space. Standardized testing for excipients could play a critical role in the definition of design space and any quality-by-design endeavor must define the materials properly. There is a growing need for a systematic process to evaluate the interaction between components of a product to increase scientific understanding and correlation between physical and mechanical properties of materials and their functionality and ways in which the design space can be expanded by development of relevant functionality tests. This symposium will address the role the functionality tests of excipients will play in the QbD world through how we perform the functionality tests, how this test helps in establishing the design space, and the appropriate control strategies. A regulatory perspective will provide insight into this concept. In addition, the challenges and opportunities facing the excipient manufacturers and also the role of the pharmacopoeia as it pertains to supporting such changes will also be discussed as part of this symposium.

# AAPS Regulatory Sciences (RS) Programming

## MODERATOR

Umang Shah, Ph.D.  
Solvay

## FDA's Perspective

Moheb Nasr, Ph.D., invited  
U.S. Food and Drug Administration

## USP Perspective on Performance Related Tests for Excipients

Kevin Moore, Ph.D.  
United States Pharmacopeia

## Excipient User's Perspective

Mohan Ganapathy, Ph.D.  
Merck and Co., Inc.

## Excipient Manufacturer's Perspective

Richard C. Moreton, Ph.D.  
Finnbrit Consulting

## WEDNESDAY AFTERNOON ROUNDTABLES

2:00 pm – 4:00 pm

### Comparator Products — Untold Stories

#### Roundtable

Conducting global clinical studies for later phases of development (Phase II – Phase III) requiring the use of comparator products presents an array of CMC challenges. These challenges are further enhanced in double-blinded studies where a placebo matching the comparator is required. Pharmaceutical companies use over-encapsulation as a tool to blind the comparator and its matching placebos. This technique has its limitations, and CMC challenges, some of which include the need for conducting BA/BE studies, setting comparators' specifications, the utility of the appropriate analytical tests and the accompanying validation studies to support these tests, and conducting the appropriate stability program to establish the shelf-life of these comparators once over-encapsulated. Pharmaceutical companies also manufacture matching placebo products that look exactly the same as the comparator product used. The main CMC challenge encountered when conducting these studies include the successful manufacture of a matching placebo with no infringement on trademarks. Additional challenges include the setting of the appropriate specifications and shelf-life for the matching placebo. Formulation changes, excipient changes, and variations in dosage strengths are also critical issues to be addressed when conducting global clinical studies. The strategy for selecting the appropriate "comparator product" requires close collaboration between regulatory, regulatory-CMC, clinical supplies operations, manufacturing, and clinical to successfully conduct these studies. This roundtable will address the blinding strategies, best practices, and inter-functional collaboration leading to the appropriate choice of comparator product and the successful conduct of these global studies.

## MODERATORS

Kim Huynh-Ba, M.S.  
PHARMALYTIK

Ruben Lozano, Ph.D.  
Bristol-Myers Squibb

## Development of Dissolution Methods for Comparator Products — The Unspoken Challenges

Qingxi Wang, Ph.D.  
Merck and Co., Inc.

## Bioavailability Challenges for Comparator Products

Dakshina M. Chilukuri, Ph.D.  
U.S. Food and Drug Administration

## Regulatory Expectations for Comparator Product Use in Clinical Trials

Speaker to be Determined

## WEDNESDAY AFTERNOON SYMPOSIA

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Because health matters

2:00 pm – 4:30 pm

### Using the Quality-by-Design Principle to Establish Pharmaceutical Equivalence and Bioequivalence of Advanced Dosage Forms

#### Symposium

With the advances in pharmaceutical science and technology, there is increasing growth in novel dosage forms and drug delivery systems. Including many modified release dosage forms, liposomal products, drug-eluting stents, and possibly nanotech-derived pharmaceuticals in the near future. Given the complexity of these advanced dosage forms, a number of challenges have been presented to industry and regulatory scientists in assessing pharmaceutical equivalence and bioequivalence, hence therapeutic equivalence. To achieve equivalence of these dosage forms, the U.S. Food and Drug Administration is currently encouraging drug sponsors to use a more systematic approach, such as quality-by-design (QbD) principle, for pharmaceutical development and manufacturing. Recently, it has been proposed that equivalence may be established by matching the test and reference *in vivo* drug delivery profiles (iDDPs) before drug absorption. With the application of QbD principle, this can be achieved by first characterizing the key component(s) of the reference iDDP and then using this information as the target for development of a test product. Critical variables or parameters may be identified to serve as *in vitro* markers or biomarkers for mapping the desired iDDP. Successful design of an equivalent test product can ultimately be accomplished with a better understanding of relevant

factors that may have potential impact on the iDDPs of products in comparison. This session will bring together pharmaceutical scientists from industry, academia; and the regulatory agency to discuss how to use QbD principle and iDDPs to demonstrate equivalence of these dosage forms pre- and post-approval, identify critical factors that may have impact on iDDPs and product quality/performance, hence equivalence of advanced dosage forms, and explore various tools to assess the iDDPs of these dosage forms.

## MODERATOR

Vincent H.L. Lee, Ph.D.  
The Chinese University of Hong Kong

## Equivalence-by-Design: Targeting Pre-absorption Drug Delivery Profiles to Ensure Equivalence

Mei-Ling Chen, Ph.D.  
U.S. Food and Drug Administration

## Critical Formulation Factors for Establishing Equivalence of Modified Release Dosage Forms

James Polli, Ph.D.  
University of Maryland

## Application of Imaging Technique in Bioequivalence Testing

Karsten Madar, Ph.D.  
Martin-Luther-University of Halle

## Biorelevant Dissolution and QbD for ANDAS

Lawrence X. Yu, Ph.D.  
U.S. Food and Drug Administration

2:00 pm – 4:30 pm

### Microdialysis Role in the Development and Optimization of Drug Topical Delivery

#### Symposium

The rapid and efficient development and evaluation of topical delivery systems is still a challenge, particularly when new approaches or devices like iontophoresis are tested. *In vivo* cutaneous microdialysis allows studying drug delivery and pharmacokinetics as close as possible to the site of action and provides a tremendous tool for a better understanding of how the formulation affects drug PK into the skin. The proposed symposium will start with an overview of the microdialysis technique as applied to skin issues and will compare it with the other methods used to study PK in skin or skin layers. Then some of the available studies that utilized MD in skin will be presented and discussed. An expert from the U.S. Food and Drug Administration (FDA) will also be invited to provide insights into the regulatory aspects of the technique. The symposium will provide the attendee with the opportunity to evaluate the contribution of MD to improve our understanding of skin delivery.

# AAPS Regulatory Sciences (RS) Programming

## MODERATORS

Caryn Purdon, Ph.D.  
Nycomed

Chinmay Shukla, Ph.D.  
U.S. Food and Drug Administration

### Microdialysis in Skin: Overview and Comparison with Other Techniques

Chris D. Anderson, M.D.  
Linköping University

### Microdialysis in the Selection of Optimal Formulations for Iontophoretic Drug Delivery

Grazia Stagni, Ph.D., M.S.  
Long Island University

### Determination of Drug Penetration in Diseased Skin

Speaker to be Determined

### The Regulatory View Point

Edward Bashaw, Pharm.D., invited  
U.S. Food and Drug Administration

## Thursday, November 12, 2009

## OPEN FORUMS

1:30 pm – 5:00 pm

### Global Regulatory Challenges for Genotoxic Impurities

**AAPS Regulatory Sciences (RS) Open Forum**  
*An additional fee is required to attend this open forum*

Controlling the quality of medicines is one of the critical aspects of assuring safety and efficacy of pharmaceutical products. The International Conference on Harmonization (ICH) has published general guidance (Q3A) on the quality and safety assessment of impurities in pharmaceutical drug substances and drug products but is not specific to Genotoxic impurities. The European Medicines Agency (EMA) has published a guideline focusing on limits for genotoxic impurities, and the U.S. Food and Drug Administration (FDA) has recently issued draft guidance on genotoxic and carcinogenic impurities in drug substances and drug product. These guidance documents have many similarities including limits based on a Threshold of Toxicological Concern (TTC) derived from animal carcinogenicity data to estimate a daily dose (1.5 µg/day) for genotoxic/carcinogenic impurities in human medicines. There are however differences including the FDA mandated genotoxic testing of impurities above the ICH qualification threshold, even in the absence of structural alerts. Presentation of the TTC as a single figure infers an unwarranted level of control and supports the adoption of a more flexible approach by regulatory

authorities when evaluating new drug products. Furthermore, the limit is based on 70 years of continuous daily exposure, a scenario that is uncommon for most medicines and not applicable to the pre-registration clinical development phase. To address this latter point, a staged TTC has been developed that proposes limits based on shorter durations of treatment, e.g., up to 1 year. Based on recent history, this approach has been acceptable to some authorities but not to others. This Open Forum will address these challenges by reviewing the current regulatory views from the US and EU and how industry has applied recent guidance globally to drug candidates in development and on established products. Questions that could be addressed in the open forum include; will a shortened duration of therapy allow for increased regulatory flexibility? How can *in silico* tools be leveraged when control strategies for genotoxics are developed? How will the current guidances be applied to innovative dosage forms (trans-dermals, depots, etc.)? What are the practical challenges to achieving TTC levels (including manufacturing processes and analytical method limitations? Should controls be different for pediatric medicines? An Expert Panel would facilitate discussion for at least 60 minutes. The discussion from the forum could be captured in a variety of publications, including the *AAPS Journal*, the *DIA Journal*, or *Regulatory Rapporteur*.

## MODERATORS

Stephen Colgan, Ph.D.  
Pfizer Global Research & Development

Ganapathy Mohan, Ph.D.  
Merck and Co., Inc.

### Control of Genotoxic Impurities and the Regulatory Impact of this: A Case Study

Ganapathy Mohan, Ph.D.  
Merck and Co., Inc.

### Continuing Challenges of GTIs

Gopi Vudathala, Ph.D.  
Sanofi-Aventis

### FDA Point of View

David Jacobson-Kram, Ph.D., invited  
U.S. Food and Drug Administration

### E.U. Point of View

Peter Kasper, Ph.D.  
Federal Institute for Drugs and Medical Devices

### Panel Discussion: Regulatory Queries and Strategies Related to Genotoxics for NCEs, Generics, and Established Products

## FACILITATOR

Stephen Colgan, Ph.D.  
Pfizer Global Research and Development

1:30 pm - 5:00 pm

## Biosimilars-Development Considerations and Future Directions

### AAPS Biotechnology Section (BIOTEC) and Regulatory Sciences (RS) Open Forum

*An additional fee is required to attend this open forum.*

As global sales for biologic products is on the rise, this market represents an attractive target for generic companies. The approaches related to biosimilar products in the various regions across the world are divergent, with a clear need for defining regulatory expectations for these products at the global level. In the USA, legal pathways exist for review and approval of some smaller, well characterized proteins such as human growth hormone and insulin, which are regulated under the Federal Food, Drug, & Cosmetic Act; however, for other biotherapeutics such as interleukins and interferons, which are regulated under the Public Health Service Act (PHSA), there is currently no abbreviated authorization pathway. However, there are signs of some momentum in this regard, with the recent support expressed by the Obama administration, and proposed legislation H.R. 1427 "Promoting Innovation and Access to Life-Saving Medicines Act." recently introduced by a bipartisan group of Congressional representatives that would open the door to approval of biosimilar products. Contrary to the USA a legal framework for biosimilars exists in the EU since the review of EU legislation. The first biosimilar product in the EU was Somatotropin / Sandoz (Omnitrope®). Countries such as China, India and South Korea also have reported a high number of licensed biosimilars within their existing regulatory framework. Examples of such products marketed in these countries include interleukins, interferons, erythropoietins, growth factors, hormones, enzymes and monoclonal antibodies. This is expected to be a topic that will be a center of debate between legislators, the biotechnology and generic industry. The open forum will feature experts who will address the regulatory framework for approval of biosimilars in the key regions, and address challenges and considerations for development of these products.

## MODERATOR

Deepa Deshpande, Ph.D.  
Universal Regulatory, Inc.

### E.U. Considerations

Marie-Christine Bielsky, M.D.  
Medicines and Healthcare Products Regulatory Agency (MHRA)