

AAPS Biotechnology (BIOTEC) Programming

AT A GLANCE

Sunday	Monday	Tuesday	Wednesday	Thursday
			7:00 am – 8:15 am SUNRISE SESSION Rational Design of a Freeze-dried Formulation for a Biologic	7:00 am – 8:15 am SUNRISE SESSION Protein-based Vaccines
8:30 am – 4:00 pm SHORT COURSE #1 RNA-targeting Therapeutics: Issues and Advances <i>An additional fee is required to attend this short course</i>		8:30 am – 11:00 am SYMPOSIUM Impact of the Variability of Ligand Binding PK Assays on the Outcome of Comparability Assessments for Follow-on Biologics AAPS Graduate Student Symposium in Biotechnology (BIOTEC) SPONSORED BY 		
		9:00 am – 11:00 am ROUNDTABLE Latest Developments of Drug Targeting to Cancer Stem Cells	9:00 am – 11:00 am ROUNDTABLES Impact of Pharmacogenomics on Drug Development: An Industrial Perspective ISR Failure: Avoiding and Resolving Through Investigation	
	2:00 pm – 4:00 pm ROUNDTABLE Strategies for the Determination of a Robust Cut Point in Immunogenicity Assays: Impact of Immunogenicity White Paper	2:00 pm – 4:30 pm SYMPOSIUM New Frontiers in Biologics: Advances & Challenges in PEGylation and Alternatives to PEGylation		1:30 pm – 5:00 pm OPEN FORUM Biosimilars-Development Considerations and Future Directions (BIOTEC & RS) <i>An additional fee is required to attend this open forum</i>
	2:00 pm – 4:30 pm MONDAY AFTERNOON SYMPOSIA FUNDED BY A GRANT FROM  SYMPOSIUM Leaner Development Strategies to Enrich Drug Pipeline			
	5:30 pm – 7:00 pm Biotechnology (BIOTEC) Section Joint Membership Meeting and Reception			

AAPS Biotechnology (BIOTEC) Programming

Sunday, November 8, 2009

8:30 am – 4:00 pm

RNA-targeting Therapeutics: Issues and Advances

Short Course #1

An additional fee is required to attend this short course

The use of oligonucleotides as therapeutic agents has elicited a great deal of interest. Basic understanding of the pharmacokinetics and delivery of antisense oligonucleotides and siRNA as tools for silencing genes or regulatory RNAs is foundational to their appropriate design and application. The short course will consist of the following lecture topics: basic knowledge of siRNA and antisense and *in vivo* uptake mechanisms/ pathways of oligonucleotide uptake into cells, overview of RNA-targeting therapeutics-basic primer, siRNA promise and challenges of RISC based targeting of mRNA, specific *in vivo* targeting of siRNA advances and challenges, antisense advances and challenges of single-strand, pharmacokinetics and ADME characterization of siRNA in animal models, pharmacokinetics and ADME characterizations of siRNA in humans, MicroRNA, a new target for RNA-targeting therapeutics, and regulatory pathways for oligonucleotide therapeutics.

MODERATORS

Pei Fan (Jane) Bai, Ph.D.
U.S. Food and Drug Administration

Richard Geary, Ph.D.
ISIS Pharmaceuticals, Inc.

Antisense/antisense: Advances and Challenges of Single-strand Antisense

Richard Geary, Ph.D.
ISIS Pharmaceuticals, Inc.

Uptake Mechanisms of Oligonucleotides

Frank Bennett, Ph.D.
ISIS Pharmaceuticals, Inc.

Therapeutic Development of MicroRNA: Promises and Challenges

Peter Linsley, Ph.D.
Merck and Co., Inc.

Progress in the Delivery of siRNA

Mark Tracy, Ph.D.
Alnylam Pharmaceuticals

Oligonucleotide Therapeutics: Regulatory Pathway

Pei Fan (Jane) Bai, Ph.D., invited
U.S. Food and Drug Administration

Clinical Pharmacokinetic and Safety Studies of RNAi in Humans

John DeVincenzo, Ph.D.
University of Tennessee Health Science Center

Monday, November 9, 2009

MONDAY AFTERNOON ROUNDTABLES

2:00 pm – 4:00 pm

Strategies for the Determination of a Robust Cut Point in Immunogenicity Assays: Impact of Immunogenicity White Paper

Roundtable

The accurate prediction of pharmacokinetic parameters in humans and anticipation of human dose (AHD) for early human studies based on preclinical and/or physicochemical data remains a major challenge, in spite of coverage of this topic in the literature and at AAPS meetings (e.g. P. Lowe et. al., *Xenobiotica*, 2007). While many methods are known, such as allometry, or physiology based pharmacokinetic modeling (PBPK), and *IV/IVC*. Many questions remain for pharmaceutical scientists on how to predict human dosing regimen for “difficult” compounds with confidence, such as those with species dependent or formulation dependent PK, i.e. BCS class II and IV compounds with solubility/dissolution limited exposure. Some companies have developed their own strategies, and others have published their methods, but often specifics are not covered in detail. In this session recent case examples for human PK and dose projections of compounds with new data will be covered. The session will focus on current compounds, and will not be a review of text book examples. The session will cover latest AHD applications using practical and tested methods, including human PK parameter projections including for clearance, (CL) distribution (Vd) and bioavailability (F). How to use multiple approaches to verify human PK parameters, and how to establish and judge confidence in predictions methods with tools such as metabolic *IV/IVC* and reverse pharmacology approaches – thus minimizing “Guesswork”. How to integrate Human PK projections with PK/PD modeling results for predicting human plasma concentration-time profiles and a suitable dosing regimen using a PBPK modeling approach. How to integrate formulation parameters into human PK profile predictions for BCS class II and IV drugs using GastroPlus. How to assess human PK profiles with new modified release formulations, with dissolution data and establish *IV/IVC* for all BCS classes. How to establish and use *IV/IVC* for new formulations of marketed drugs or drugs in clinical trials. This event will benefit all pharmaceutical scientists who are involved with first-in-human (FIH) dose projections, or are in early to late development, where human PK and dose projections are sought. This event will cover latest trouble-shooting, modeling, and *IV/IVC* strategies that have been successfully used.

MODERATOR

Masood U. Khan, Ph.D.
Covance Laboratories, Inc.

Cut-point Determination: Impact of Immunogenicity White Paper and Current Industry Practices

Gopi Shankar, Ph.D.
Centocor R & D

A Statistical Primer to Deal with the Cut-point Issues

Viswanath Devanarayan, Ph.D.
Abbott Laboratories

Presentation Title to be Determined

Speaker to be Determined
U.S. Food and Drug Administration

MONDAY AFTERNOON SYMPOSIA

FUNDED BY A GRANT FROM



2:00 pm – 4:30 pm

Leaner Development Strategies to Enrich Drug Pipeline

Symposium

The pharmaceutical industry is facing rising challenges of enormous drug development costs. It is highly desirable to reduce development cost and time for early stage drug candidates and delay major investments to later stage. However, it is also critical to ensure quality and safety of early stage drug products. To achieve cost-effectiveness, a good balance is to employ smart approaches such as high-throughput analytical assays, faster formulation screens, and platform experimental protocols. Obviously, technological advancements play key role to accomplish such audacious goals. This session will focus on high-throughput analytical assays, automated techniques, and minimizing API consumption. Development of key stability-indicating methods, smarter formulation screens as opposed to successive ones, platform process for drug product manufacturing, and predictive stability.

MODERATORS

Tapan K. Das, Ph.D.
Pfizer, Inc.

Satish Singh, Ph.D.
Pfizer, Inc.

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Platform Process for Drug Product Development and Manufacturing — Cycle Time and Resources

Nicholas Warne, Ph.D.
Wyeth

Predictive Stability to Accelerate Biotherapeutics Development

Tapan K. Das, Ph.D.
Pfizer, Inc.

Novel Methods for Accelerating Formulation Development of Biotherapeutics

Judy Chou, Ph.D.
Genentech, Inc.

High Throughput Formulation of Biopharmaceuticals: Case Studies

Tudor Arvinte, Ph.D.
School of Pharmaceutical Sciences, University of Geneva & University of Lausanne

JOINT MEMBERSHIP MEETING AND RECEPTION

5:30 pm – 7:00 pm

Biotechnology (BIOTEC) Section Joint Membership Meeting and Reception

Tuesday, November 10, 2009

TUESDAY MORNING SYMPOSIA

8:30 am – 11:00 am

Impact of the Variability of Ligand Binding PK Assays on the Outcome of Comparability Assessments for Follow-on Biologics

Symposium

Manufacturing changes are frequently introduced during the lifecycles of biologic products to continue to improve their quality and/or processes. However, due to the heterogeneity and complexity of biologic products and the manufacturing processes, batch to batch differences are expected. Demonstration of product comparability is necessary to show that these modifications have no adverse impact on the quality, safety and efficacy of the biologic product before implementation of the changes. Ideally, if product comparability can be established through *in vitro* analytical testing, nonclinical, and clinical studies are not warranted. However, when the relationship between specific quality attributes and safety and efficacy has not been established, and differences between quality attributes of the pre-and post-change product are observed, nonclinical and/or clinical studies may be warranted to provide the assurance of comparability of pre-

and post-modification products. Ligand binding or functional assays are often used for quantification of biotherapeutics in biologic matrices to support PK characterization. Due to the heterogeneous nature of biologic products and/or key reagents (antibodies), the performance of binding or functional assays can have a direct impact on the study design and the outcome of comparability assessment. This symposium will provide the statistical bases on how assay performance impacts study design as well as case studies provided by both regulators and researchers from pharmaceutical/biotech companies.

MODERATORS

Marie T. Rock, Ph.D.
Midwest BioResearch LLC

Huifen F. Wang, Ph.D.
Pfizer, Inc.

Regulatory Considerations Related to Follow-on Protein Products

Speaker to be Determined
U.S. Food and Drug Administration

Connecting the Dots: Integrating Assay Performances in the Clinical Development Plans

Bruno Boulanger, Ph.D.
UCB

Ligand Binding Assays Supporting Comparability Studies of Macromolecules — Can We Confirm what We are Measuring in the Absence of Orthogonal Methods?

Binodh DeSilva, Ph.D.
Amgen Inc.

Biosimilars, Follow on Biologics, and Bioequivalence: A Study of Recombinant Versus Plasma Derived Factor Replacement Therapies

Ann Gooding
Wyeth

GRADUATE STUDENT SYMPOSIUM

8:30 am – 11:00 am

AAPS Graduate Student Symposium in Biotechnology (BIOTEC)

SPONSORED BY



TUESDAY MORNING ROUNDTABLES

9:00 am – 11:00 am

Latest Developments of Drug Targeting to Cancer Stem Cells

Roundtable

It has been increasingly evident that cancer is probably initiated from and maintained by a small sub-population of undifferentiated, tumorigenic cells called cancer stem cells (CSCs). Production of the main mass of the tumor may be attributed to this minor population of CSCs through a particular process of continuous self-renewal and differentiation. Thus, CSCs have come into sight as a potential target of cancer therapy. Up to date, many types of cancer stem cells have been identified in various cancers including breast, colorectal, pancreatic, head and neck cancers. Since cancer stem cells are resistant to current available chemotherapeutic regimen, it is important to explore new molecular target to eliminate these drug resistant cancer stem cells. In this roundtable, we will provide a forum to debate cancer stem cell concept, targeted drug delivery and drug targeting strategy to eliminate cancer stem cells.

MODERATORS

Duxin Sun, Ph.D.
University of Michigan

Tycho Heimbach, Ph.D., M.S.
Novartis

Cancer Stem Cells: The Emerging Challenge of Drug Targeting

Maguer-Satta Véronique, Ph.D.
Léon Bérard Multidisciplinary Center

Targeting Breast Cancer Stem Cells

Suling Liu, Ph.D.
University of Michigan

Targeted Therapy and Chemoprevention for Cancer Stem Cells

Duxin Sun, Ph.D.
University of Michigan

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TUESDAY AFTERNOON SYMPOSIA

2:00 pm – 4:30 pm

New Frontiers in Biologics: Advances & Challenges in PEGylation and Alternatives to PEGylation

Symposium

Biotechnology derived drugs have become a significant proportion of marketed therapeutic drugs. Traditional monoclonal antibodies as the classical members of therapeutic biologics bind to targets with high specificity. However, they are complex, expensive to manufacture, and have immunogenicity issues. A need for more efficient and cost-effective alternatives has led to the development of a new class of protein scaffolds ca. antibody fragments that retain the binding properties and are easier to process. But these alternatives suffer from the loss of desirable PK properties due to their small size. PEGylation has been classically used to improve the plasma half-life, increase bioavailability, decrease immunogenicity, and enhance solubility and stability. Nonetheless, there are inherent challenges associated with the use of PEG. Several newer alternatives to PEGylation are emerging with great potential to solve these issues. This symposium is designed to review the latest advances in pharmaceutical development of biologics. Particularly, this symposium will cover the advances and challenges associated with PEGylation of biologics. Some alternative technologies to PEGylation to achieve the desirable properties will be discussed as well. This symposium will benefit anyone interested in learning the advances in developing PEGylated protein drugs.

MODERATORS

Rajesh B. Gandhi, Ph.D.
Bristol-Myers Squibb

Pankaj V. Paranjpe, Ph.D.
Bristol-Myers Squibb

PEGylated Proteins: An Updated Review

Francesco M. Veronese, Ph.D.
Padova University

Challenges in the Downstream Processing of PEGylated Products

Peter Ihnat, Ph.D.
Bristol-Myers Squibb

Analytical Resolution of PEGylated Proteins

Anna-Maria A. Hays Putnam, Ph.D.
Ambrx, Inc.

Genetic Engineering Approaches to Enhance Half-life of Proteins

Volker Schellenberger, Ph.D.
Amunix, Inc.

Wednesday, November 11, 2009

WEDNESDAY SUNRISE SESSIONS

7:00 am – 8:15 am

Rational Design of a Freeze-dried Formulation for a Biologic

Sunrise Session

Approaches to freeze-dried formulations are often empirical or semi-empirical and frequently overlook the intimate relationship between the formulation, the freeze-drying process, and the package. This session will outline the basic precepts that need to be considered when developing a freeze-dried protein candidate. Emphasis is also placed on reducing commonly encountered freeze-drying problems and cycle time through judicious use of excipients, packaging, and processing considerations.

MODERATOR

Lavinia M. Lewis, Ph.D.
Pfizer, Inc.

Rational Design of Freeze-dried Formulation for a Biologic

Dirk Teagarden, Ph.D.
Pfizer, Inc.

WEDNESDAY MORNING ROUNDTABLES

9:00 am – 11:00 am

Impact of Pharmacogenomics on Drug Development: An Industrial Perspective

Roundtable

Pharmacogenomics has emerged as an important tool for discovering new therapeutic agents as well as re-evaluating existing drugs for improving their efficacy and/or applications. The pharmaceutical industry continues to contribute significantly to development of high-throughput technologies applied to pharmacogenomic research. Efficient translation of the scientific data into clinical applications requires careful analyses, prioritization and streamlining of the information at various levels even as the regulatory approvals are sought. While pharmaceutical organizations follow their own set of internal standard operating protocols and process guidelines, it would be useful to provide a common platform to researchers from the industry to share their experiences and perspectives on what strategies worked, how challenges were overcome, what do they foresee as emerging issues in the near future, and what is the impact of the pharmacogenomic approach on the overall economics of the drug development/approval process.

MODERATORS

Lawrence Fleckenstein, Pharm.D.
University of Iowa

Pramod Mahajan, Ph.D.
Drake University

Impact of Pharmacogenomics on Drug Development: An Industrial Perspective

Allen Roses, M.D.
Cabernet Pharmaceuticals Inc.

Impact of Pharmacogenomics on Drug Development: A Medco Perspective

Felix Frueh, Ph.D.
Medco Health Solutions, Inc.

Impact of Pharmacogenomics on Drug Development: A Lilly Perspective

Sandra Close Kirkwood, Ph.D.
Eli Lilly and Co.

9:00 am – 11:00 am

ISR Failure: Avoiding and Resolving through Investigation

Roundtable

In 2006 the U.S. Food and Drug Administration (FDA) presented guidance instructing the pharmaceutical industry to perform sample re-analysis for regulated studies to ensure method reproducibility. In February of 2007, AAPS hosted a workshop specifically designed for the open discussion of Incurred Sample Reanalysis (ISR) and to implement a standard, industry wide practice. As part of this guidance, failure of ISR could lead to a full stop on study sample analysis until an investigation is satisfactorily conducted as to the cause and resolution of the discrepancy. These investigations may have significant consequences including delaying a therapeutics' release to market. The purpose of this roundtable is to discuss strategies to avoid a failure of ISR as well as different approaches to conducting a successful investigation when necessary.

MODERATOR

Suzanne Brignoli
Genentech, Inc.

Investigative Procedures When ISR Fail

Dick Tacey, B.S.
PPD, Inc.

ISR Failure Investigation: Strategies to Avoid Failure and Increase Success

Joseph F. Bower, Ph.D., M.B.A.
Covance Laboratories

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Thursday, November 12, 2009

THURSDAY SUNRISE SESSIONS

7:00 am – 8:15 am

Protein-based Vaccines

Sunrise Session

An introduction to protein-based vaccines platform and the challenges associated with development. This session will introduce the platforms (antigenic proteins, VLPs, conjugates, etc.), their use, mechanisms of action, characteristics, and a survey of current state of preclinical and clinical development.

MODERATOR

Satish Singh, Ph.D.
Pfizer, Inc.

Protein-based Vaccines Platforms

Indresh Srivastava, Ph.D.
Novartis

OPEN FORUM

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)

Legal and IP Issues for Biosimilars

Anie Roche, Ph.D.
Wilson, Sonsini, Goodrich and Rosati

Presentation Title to be Determined

Islah Ahmed, M.D.
Hospira, Inc.