

Conference Program - SUNDAY & MONDAY

Sunday, June 24

7:00 am – 5:00 pm

Registration

Monday, June 25

7:30 am – 5:30 pm

Registration

8:30 am – 11:30 am

Plenary Session

Welcome and Opening Remarks

Ronald R. Bowsher, Ph.D.
B2S Consulting LLC, and
LINCO Diagnostic Services, Inc.
... a Millipore Company

Opening Remarks and Presentation of Chair's Plaque

Eugene F. Fiese, Ph.D.
2007 AAPS President.

Moderator

Ronald R. Bowsher, Ph.D.
B2S Consulting LLC, and
LINCO Diagnostic Services, Inc.
... a Millipore Company

Steven F. Dowdy, Ph.D.
USCD School of Medicine

Stanley T. Crooke, M.D., Ph.D.
Isis Pharmaceuticals, Inc.

Daria Mochly-Rosen, Ph.D.
Stanford University

12:00 pm – 6:30 pm

Exhibits

12:00 pm – 6:30 pm

Contributed Papers Session I

Authors will be present at their boards from
5:00 pm – 6:00 pm

1:00 pm - 3:30 pm

**Perspectives on Biomarker
Assay Translation from Drug
Discovery to Clinical Diagnostics**

Symposium

Co-sponsored with AACC

Session Description to be Announced

Biomarker Assay Development and Validation – Pharma/Biotech Perspective

John A. Wagner, M.D., Ph.D.
Merck Research Laboratories

Biomarker Validation for Routine Clinical Testing

Dennis J. O'Kane, Ph.D.
Mayo Clinic

How Do We Partner to Provide Patients What They Want and Need?

Robert Dean, M.D., Ph.D.
Eli Lilly and Company

1:00 pm - 3:30 pm

**Nanomaterial Pharmacokinetics
and Toxicology**

Symposium

Nanomaterials are engineered structures with at least one dimension of 100 nanometers or less. These nanoscale materials often have unique chemico-physical properties that are different from those of their larger counterparts. Possible undesirable results of these unique properties are harmful interactions with biological systems and the environment, with the potential to generate toxicity. There is a great need for determination of biodistribution and pharmacokinetics, as well as safety evaluations for nanomaterials. A major difficulty is the proper method of quantitation. The symposium brings together scientists to share their research in identifying problems and issues pertaining to pharmacokinetics and toxicity assessments of nanomaterials. The purpose of this symposium is to highlight the current knowledge and emphasize the challenges of research in nanomaterials. A better understanding of the modes of action for nanomaterials is important. The approaches to facilitating the development of appropriate hazard data and collection of accurate human and environmental exposure information will be discussed.

Moderators

K. Sandy Pang, Ph.D.
University of Toronto

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

1:00 pm - 3:30 pm

**Use of Protein Arrays and
Cytoscape in Mapping Cellular
Protein-protein Interactions**

Symposium

With recent advances in proteomics, it is only a matter of time before protein arrays are acknowledged by the pharmaceutical industry. Compared with approximately 25,000 genes in the genome, the human proteome is predicted to exceed 1 million, which is even further complicated by more than 300 known post-translational modifications (Celis 2004). Recently, miniaturized protein array technology has shown a great potential for rapid and efficient identification of protein targets. Numerous applications for this technique regarding protein-protein, -peptides, -low-molecular weight compounds, and -DNA interactions have been reported recently. These arrays can also be used to screen post-translationally modified proteins for interaction with the above-mentioned compounds. The real task following identification of target proteins begins with investigating protein-protein interactions and answering the questions concerning how proteins communicate with each other inside of an intact cell. Cytoscape, is an open-source program that can be used to visualize and analyze the interaction network inferred from protein array experiments. (Shannon et al. 2003). More investigation into these interactive networks provide new perspectives on human diseases and the drug design. This high-throughput systems approach should be introduced into drug design as a supplement to the current approach of focusing on a one single protein and designing drugs for a single target.

Moderator

Nazila S. Miller, Ph.D.
University of Kansas

**Using Cytoscape to Visualize and
Analyze Protein Interaction Network**

Michael Smoot
University of California

Additional Titles and Speakers to be Announced

1:00 pm - 3:30 pm Phase IV Requirements for Therapeutic Biologics

Symposium

The FDA is increasingly keen about post-marketing safety data and capturing events that might have been missed during the drug development phase. Some therapeutic biologics are approved for unmet needs on a fast track with limited clinical experience. As approval of biosimilar/follow-on products is gaining momentum, Phase IV studies to capture rare safety events may become crucial as part of post-marketing programs. Therefore it is imperative to examine the current post-marketing requirements for therapeutic biologics including follow-on biologics. In this session, Phase IV requirements on safety and immunogenicity assessments will be the primary focus.

Moderators

Sanjay Sehgal, Ph.D.
Wyeth Research

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

Post-marketing Formulation Changes for Biologics: Can Population Analyses Help?

Jogarao Gobburu, Ph.D.
U.S. Food and Drug Administration

Types of Phase IV Commitments for Biologic Registrations—FDA Experience

Cristi Stark, M.S.
U.S. Food and Drug Administration

Post-approval Studies for Biosimilar Products

Alexander Berghout, M.D., Ph.D.
Sandoz

3:30 pm - 5:00 pm Challenges of Re-analysis of Macromolecular Therapeutics in Study Samples

Roundtable

When analyzing samples in a GxP environment, especially when supporting a regulatory filing, it is desirable to have only a 'single result' for a given sample. However, analytical chemists are confronted with sample re-analysis quite frequently. A confounding challenge lies in the decision to select and report a result when multiple valid results are obtained for a given

sample. Scenarios that may lead to re-analysis of a sample, especially for immunoassays, may include: (a) over or under dilutions, (b) failed analytical runs, (c) technical errors, (d) high CVs between replicates, (e) sample management errors, (f) PK outliers, or (g) anomalous results. Moreover, during the 3rd Crystal City Workshop on Quantitative Bioanalytical Method Validation and Implementation (May 1-3, 2006), it became apparent that the regulatory agency may expect routine re-analysis of a certain number of study samples to demonstrate method repeatability. However, reproducibility of results, especially where macromolecular therapeutics are involved, may depend on several factors (e.g. freeze-thaw stability, storage temperature and duration, non-specific matrix effect, etc.) other than the reproducibility of the method per se. Typically, result reporting processes are defined *a priori* in some form of Standard Operating Procedure. Also, a variety of decision trees for selecting a reportable result out of multiple valid results are in use throughout the industry. However, there is a lack of standardization in these practices. This roundtable will focus on current industrial approaches for selection of reportable results resulting from sample re-analysis and the potential harmonization of the process. An attempt will also be made to further define the ground rules for dealing with, and managing, the challenging proposition regarding regulatory expectations of routine study sample re-analysis.

Moderators

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

Jeffery M. Sailstad
Trimeris

Re-analysis of Study Samples: Challenge of Reporting the Results

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

Re-analyzing the Study Samples: An Industry Perspective

Mario L. Rocci, Ph.D.
Prevalere Life Sciences

Title to be Announced
Patrick G. Swann, Ph.D. (*invited*)
U.S. Food and Drug Administration

3:30 pm - 5:00 pm IgG Subclass and Antibody Based Therapeutics

Roundtable

Immunoglobulin G (IgG) is the backbone of most antibody-based therapeutics. IgG is composed of four different subclasses (IgG1, IgG2, IgG3 and IgG4). Antibody framework is critical and important for monoclonal antibody therapeutic development. Subclasses of IgG not only display substantial differences in their ability to mediate effector responses, but also have different unique molecular structures which lead to different pharmacokinetic profile. We propose a roundtable on this topic would include talks on: 1) immunobiochemistry of IgG and mediate effects of different IgG subclasses; 2) how to utilize and eliminate ADCC effect of antibody to develop an ideal therapeutic to meet the medical needs; 3) IgG subclasses and their pharmacokinetics; and 4) unique feature of IgG4: bispecificity, monovalency and *in vivo* molecular shuffling.

Moderators

Patrick M. Liu, M.D., Ph.D.
Tanox, Inc.

Wayne Gordon, Ph.D.
Tanox, Inc.

Optimization of Antibody Mediated Cell Killing

Roy Jefferis, Ph.D., D.Sc.
University of Birmingham, UK

Unique Feature of IgG4: Biospecificity, Monovalency and It's Molecular Shuffling

Patrick M. Liu, M.D., Ph.D.
Tanox, Inc.

Engineer Antibody Fc Variant with Improvement of Its Pharmacokinical

Speaker to be Announced

3:30 pm - 5:00 pm Scientific and Regulatory Considerations for the Registration of Biosimilars/ Follow-on Proteins

Roundtable

As the initial wave of biopharmaceuticals is reaching the end of their patent life, momentum is quickly picking up for the development and registration of biosimilars/follow-on proteins. With recent approval of OMNITROPEÛ, generic as well as brand name product manufacturers are showing increased interest in developing biosimilars/follow-on proteins. However, the pathways for the registration of some of these products are

MONDAY & TUESDAY

not well defined. EMEA in Europe recently issued general as well as individual therapeutic protein specific guidances and FDA is working on some general guidances. Risks (e.g., immunogenicity) associated with changes in protein products are a potential safety and efficacy concern. Use of advanced techniques in protein analysis and structural elucidation may reduce some of these uncertainties about comparability. This session will discuss: 1) global regulatory/legislative pathways currently available; 2) current FDA initiatives to address biosimilars/follow-on proteins; and 3) adequacy of scientific methodologies useful for comparative characterization of therapeutic proteins for registration purposes.

Moderators

Raja Velagapudi, Ph.D.
Barr Laboratories

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

Global Registration of Biosimilar Products

Ajaz S. Hussain, Ph.D.
Sandoz

U.S. Regulatory Considerations/ Guidances for the Registration of Biosimilars and Follow-on Proteins

Steven Kozlowski, M.D.
U.S. Food and Drug Administration

3:30 pm – 5:00 pm Exenatide

Hot Topic

Titles and Speakers to be Announced

Exenatide is the first in a new class of medicines known as incretin mimetics and was approved for use in the United States by the U.S. Food and Drug Administration in April 2005 for the treatment of type 2 diabetes. Exendin-4, the naturally occurring form of exenatide, was originally isolated from the salivary secretions of the lizard *Heloderma suspectum* (the Gila monster). Exenatide is a 39-amino acid peptide that exhibits many of the same glucose lowering effects as the human incretin hormone glucagon-like peptide-1 (GLP-1). These actions include glucose-dependent enhancement of insulin secretion, suppression of inappropriately high glucagon secretion, and slowing of gastric emptying.

Exenatide's glucose dependent action may be mediated by exenatide binding to the pancreatic GLP-1 receptor. This session will summarize key aspects of the nonclinical, bioanalytical, and clinical development program for this peptide therapeutic.

5:30 pm – 6:30 pm Welcome Reception

Tuesday, June 26

7:00 am – 5:00 pm Registration

7:30 am – 9:00 am Mentoring Breakfast

9:30 am – 6:30 pm Career Center

9:30 am – 6:30 pm Exhibits

9:30 am – 12:00 pm Contributed Papers Session I Conclusion

7:30 am - 8:30 am Population PK of Monoclonal Antibodies

Sunrise Session

The objective of this course is to provide the audience with understanding of the utility of population PK for drug development of monoclonal antibodies (MAbs): a) characterize unique PK behavior of monoclonal antibodies with Pop PK approach; b) half life and covariate effects for monoclonal antibodies; c) impact of Pop PK analysis for the drug label of MAbs; and d) impact on drug development of monoclonal antibodies. Population PK analysis has been widely used in the pharmaceutical industry. Recently, the applications of Pop PK for monoclonal antibodies in drug development increase quickly with more monoclonal antibodies moving to the late stage development and for FDA approvals. Comparing to small

molecules, MAbs have unique PK behavior such as long half life, nonlinearity caused by receptor mediated clearance and pathophysiological effect, etc. Although most companies have in-house expertise on M&S, most big pharmaceutical companies or small biotech companies might not have experience with Pop PK of monoclonal antibodies. This session will review three topics covering uniqueness of population PK analysis for MAbs and its impact on drug development of MAbs. Thus, this session will help provide the education of the PK of MAbs and generate awareness among biotech companies of using Pop PK approach to help drug development of MAbs. In addition, graduate students and trainees in pharmaceutical sciences may benefit from obtaining a basic understanding of Pop PK analysis and the PK of MAbs.

Moderator

Jianfeng Lu
Amgen, Inc.

Pop PK Examples
Philip Lowe, Ph.D.
Novartis Pharmaceuticals

Pop PK Examples
Tom Sun, Ph.D.
Amgen, Inc.

7:30 am - 8:30 am Toxicity/Toxicokinetic Considerations for Biotechnology Products: Challenges and Minimizing Risk

Sunrise Session

The integration of pharmacokinetics into toxicity studies, (i.e. toxicokinetics) will provide many new ways for the non-clinical safety departments to evaluate new products and to establish better guidelines and recommendations to senior management. In the safety assessments of biotechnology products one of the most variable issues is the conformational structure of the active moiety and the need for confirmatory PK to drive the interpretation of toxicities is the mathematical transform of PK data as applied as TK data. Toxicokinetics provides a means to produce multiple dose pharmacokinetic studies and couple the exposure to observations of injury or change in organ/tissue function. The mathematical

treatment of time-toxicity data allows for better safety assessments and prediction of clinical behavior when mapped using body surface area or allometric weighting. These data also become more relevant to the eventual clinical experience and can provide valuable translation of effort back to non-clinical development should that become necessary. The continuous feedback from clinical experience needs a mathematic relational language to describe toxicity in terms which can be modeled and communicate specific parameter estimates such as the C_{max}, AUC and MRT as quantitative toxicologic terms. The objectives of the session will be to: 1) describe systemic exposure and consequences of exposure in terms of PK; 2) describe non-clinical findings in a manner consistent to relate to clinical experience, 3) to support the choice of species as may be related to human exposure and, 4) provide a database which supports all future non-clinical study designs. The session will focus on the quantitative measures of time-exposure-pathology, examine the decision process which drives the choice of time points, the species selection issues for certain types of biotechnology products, and the appropriate TK parameters to use for selected biotechnology products.

Moderators

Brian R. Moyer, M.S.
Certus International

Joseph Balthasar, Ph.D.
University at Buffalo

Case Studies in Toxicokinetics of MABs

Anne M. Pilaro, Ph.D. (*invited*)
U.S. Food and Drug Administration

Toxicokinetics of Recombinant Products

Philip Lowe, Ph.D.
Novartis Pharmaceuticals AG

7:30 am - 8:30 am

In-Vitro and Ex-Vivo Cell Stimulation Biomarker Assays for Drug Discovery and Development

Sunrise Session

Understanding the mechanism of drug interaction or drug impact via biomarkers in molecular and cellular levels have for many years been studied in cell systems as they are less complex. However the question of whether it is applicable to targeted disease population needs to be answered. In recent years, the

perturbations introduced *in-vitro* or *ex-vivo* on special human/animal cell lines or healthy donor samples to quantitatively measure differentiating biomarker responses have been increasingly used to bridge the gap. Wide ranges of technology platforms applied to quantify the biomarker responses include ELISA, flow cytometry, microarrays of nucleic acids or proteins, and novel in-situ fluorescence. As result, the selections of cell lines and the stimuli, the optimization of the stimulation, sample handling, sample storage and assay conditions and throughput become extremely critical. This session will focus the strategies employed and practical issues involved in utilizing and developing *in-vitro* and *ex vivo* stimulation assays for support of drug discovery and development.

Moderators

Jean Lee, Ph.D.
Amgen, Inc.

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

Validation and Application of Ex-vivo Blood Stimulation Assays in the Development of Cancer Therapeutics

Robert Millham
Pfizer, Inc.

Biochemical Coverage in Early Drug Development

Dan Fitzpatrick, Ph.D.
Amgen, Inc.

9:00 am - 11:30 am

“Smart” Drug Delivery Systems: Interfacing Biotechnology with Nanotechnology to Improve Drug Therapy

Symposium

Recent advances in nanotechnology have demonstrated the feasibility of miniature devices for drug delivery applications. To fulfill the dream of personalized medicine, however, those devices require an ability to adjust dosage to an individual patient's response using intelligent biosensors. Biotechnology-based products such as peptides and proteins exhibit unique structural features that can be explored as building blocks for intelligent biomaterials to functionalize nano-sized drug delivery devices with bioresponsive sensors. The objective of the symposium is to outline the current status of “smart” drug delivery device development and

demonstrate through selected case studies the opportunities for unique collaborations between biotechnology, nanotechnology engineering, and drug delivery.

Moderators

Giovanni M. Pauletti, Ph.D.
University of Cincinnati

Shirley X. Wu, Ph.D.
University of Toronto

Nanotechnology and Intelligent Systems in Drug Delivery

Nicholas A. Peppas, Ph.D.
The University of Texas at Austin

Genetically Engineered Thermoresponsive Biopolymers: A New Paradigm for Macromolecular Drug Delivery

Darin Y. Furgeson, Ph.D.
University of Wisconsin-Madison

Responsive and Autonomous Pulsing Hydrogels: Sensing, Drug Delivery, and Microfabrication

Ronald A. Siegel, Sc.D.
University of Minnesota

Lipid-based Vectors for Gene and Drug Delivery: From Lipid-DNA Complexes with Honeycomb Structures to Lipid-protein Bio-nanotubes

Cyrus R. Safinya, Ph.D.
University of California, Santa Barbara

9:00 am - 11:30 am

Progress in Epigenetic Therapies Symposium

Only a small percentage of the genome is actually used for the transcription and resulting synthesis of proteins. Much of the genome functions in a regulatory manner, influenced by such processes as histone acetylation. Substances that influence histone acetylation, therefore, have the potential to influence the regulation of transcription and to act as therapeutic agents. The discovery of such substances, their pharmacologic properties, and potential for development as drugs will be discussed.

Moderator

Robert L. Chapman, Ph.D.
Midwestern University Chicago College of Pharmacy

Pharmacogenetics and Approaches to Treatment

Joni L. Rutter, Ph.D.
National Institutes of Health

Technological Advances in Therapeutic Decision Making

Lance Liotta, M.D., Ph.D.
George Mason University

Histone Deacetylase Inhibitors and Epigenetic Regulation

Roderick H. Dashwood, Ph.D.
Oregon State University

9:00 am - 11:30 am Innovations in Excipient Selection for Biopharmaceutical Formulation Development

Symposium

Engineering biopharmaceutical stability is widely recognized as a key aspect of product development. Both during storage as well as delivery, biotherapeutics have been known to undergo degradations, physical as well as chemical. These instabilities can reduce their potency, increase the risk of adverse events in patients, and therefore weigh in significantly on regulatory approval. One important tool that has been employed in order to preserve the identity of the drug under consideration has been to add one or more stabilizing excipients to the formulation. Broadly, biotherapeutic instability can be divided into two classes – physical (such as aggregation and fragmentation), and chemical (such as oxidation and isomerization). This symposium will feature excipient designs that prevented several aspects of biotherapeutic instability. Excipient design proposals for biotherapeutics will be expanded to include peptides, globular proteins, antibodies and fusion proteins. Depending on the dosage form (liquid or lyophilized), different excipients must be considered. Recent scientific developments in choosing excipients based on the dosage form will be included. Regulatory concerns, such as immunogenicity and delivery device compatibility will also be addressed. Finally, proposals for stabilizing excipients for high therapeutic concentration formulations will also be examined.

Title to be Announced
Bernhardt L. Trout, Ph.D.
Massachusetts Institute of Technology

Title to be Announced
Steven J. Shire, Ph.D.
Genentech, Inc.

The Role of Excipients in Modulating Stability of Proteins towards Aggregation

Rahul S. Rajan, Ph.D.
Amgen, Inc.

9:00 am - 11:30 am Embryonic Stem Cells in Drug Discovery

Symposium

Functional assays are used at various stages of drug discovery and development in target identification; target validation; library screening for early hits and leads; and for more detailed pharmacological analysis, which is required at the stages of lead optimization and drug candidate selection. Generally cell culture models are derived from tumor lines or cells immortalized by genetic transformation. These cell lines are genetically abnormal, often having abnormal karyotype, usually not of human origin, and their phenotype, even before immortalization, is usually unrelated to the phenotype of the tissue of interest. As a result the cells are unlikely to express the appropriate signaling systems in relation to the target receptor. Embryonic stem cells (ESCs) will become a source of all adult differentiated cells once reliable protocols for directed differentiation have been established. This resource will revolutionize laboratory cell biology and will provide much improved cell culture models for discovery and development of drugs, and fundamental studies of the genetic basis of disease. Once differentiation can be controlled in a reproducible manner it will be possible to run screens using normal differentiated human cells which express the appropriate signal transduction systems. There are many other potential uses for cells derived from embryonic stem cells (ESCs), such as culture of human hepatocytes for studies of drug metabolism, use of ESC for safety and toxicology assessment, and use of differentiated cells for identification of surrogate biomarkers. By genotyping the ESCs it will be possible to examine the role of human genetic variation in response to drugs, and to examine the mechanisms which control individual genetic predisposition to disease.

Moderator

Colin W. Pouton, Ph.D.
Monash University

Challenges and Opportunities

Colin W. Pouton, Ph.D.
Monash University

Models for High-throughput Screening Applications

John McNeish, Ph.D.
Pfizer, Inc.

Discovery and Design of Low Molecular Weight Differentiating Agents

Sheng Ding, Ph.D.
The Scripps Research Institute

Harnessing Human ES Cells as a Source of Cell Models

Martin Pera, Ph.D.
University of Southern California

Engineering ES Cells for Applications in Drug Discovery

Lilian Hook, Ph.D. (invited)
Stem Cell Sciences

9:00 am - 10:30 am Challenges and Opportunities for Development and Registration of Biologic Drug-device Combinations

Roundtable

Many of the new biologic drugs are being developed in combination with devices. The advantages of drug-device combination products include patient convenience, home administration and reducing risks of incorrect dosing or compromised sterility. At the same time, combination products can raise difficult development and registration challenges, since biologics and devices each have their own development paradigms and regulatory requirements. The panelists in this roundtable will discuss special considerations in developing biologic drug-device combination products and regulatory considerations for approval. Speakers will provide industry and regulatory perspectives by sharing challenges and learnings from approved products, and highlight areas for further discussion from regulatory guidances and product development experiences.

Moderators

Manpreet-Vick S. Wadhwa, Ph.D.
Amgen, Inc.

Sandeep S. Nema, Ph.D.
Pfizer, Inc.

Special Challenges in Developing Biologic Drug-device Combination Products

Cynthia Stevenson, Ph.D.
Nektar Therapeutics

U.S. Food and Drug Administration Perspectives on Biologics-device Combination Products

James Cohen, Ph.D.
U.S. Food and Drug Administration

Regulatory Challenges in Developing a Biologic-autoinjector Combination Product

Sandeep Kumar, Ph.D.
Amgen, Inc.

9:00 am - 10:30 am Challenges of Using Ligand-binding Assay for Evaluation of Vaccine Immune Response: Standardization and Validation of Analytical Assays

Roundtable

In the past 10 years there has been a steady increase in number of programs addressing macromolecular therapeutics immunogenicity (an undesired response). However, despite the increasing number of candidate vaccines (especially in response to fight against bio-terrorism) there had been very little focus on specific issues related to the characterization of 'desirable immunogenicity' of vaccine entities. The "tools" and methods may be the same but the experimental protocol, data interpretation and method validation can be quite different for immunogenicity evaluation for macromolecular therapeutics and characterization of immune response for vaccine. Vaccine development scientists have been using ligand-binding assays (LBA) in various forms to determine the efficiency, potency and characteristics of vaccine candidates. During preclinical and clinical trials, binding assays, including antibody (Ab) titer assays, cell-based neutralizing Ab and functional assays provide a critical tool in evaluating the vaccine immune responses. These assays present complex analytical

challenges primarily due to a lack of standardized assay protocol (e.g., endpoint-, midpoint-, 10 percent maximum specific binding-titer, etc.), heterogeneity of reference calibrator and control material, and non-harmonized definition of assay performance parameters. In view of this there is a need for both protocol harmonization and regulatory guidance on selection of standardized assay protocols and of specific assay performance guidelines. This roundtable will focus on the current industrial perspectives and approaches for the validation of vaccine immunogenicity detection assays. It is desirable that this will be the catalyst to begin building consensus among industrial and regulatory scientists.

Moderators

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

Boris M. Gorovits, Ph.D.
Wyeth Research

Cytokine Neutralization Assays Used for Safety Evaluation of Vaccine Trials with Cytokine Adjuvants

Ralph Braun, Ph.D.
Wyeth Research

Development and Qualification of Multiplex Luminex Based Assay for Detection of IgG Antibodies to Streptococcus Pneumoniae Capsular Polysaccharides in Human Serum

Danka Pavliakova
Wyeth Research

Standardization of Ligand-binding Assays Used for Vaccine Efficacy Determination: An Overview of Current Practices

John Leete, Ph.D.
Covance Laboratories, Inc.

9:00 am - 10:30 am Packaging – The Challenge for Biopharmaceuticals

Roundtable

In biopharmaceutical products surely the primary packaging is of high importance for functionality and quality of the drug product

and is comparable to the significance of the composition of the medicament. Since biopharmaceuticals are mostly parenterally used, the guaranteed microbiological status through tight closure is indispensable. Due to the high price level of biopharmaceutical drugs, packaging defects must be avoided by appropriate quality and incoming inspection of packaging components, since every rejected container after filling represents a substantial cost factor. Also, the sensitive active ingredients should not be affected by interactions with the packaging material nor by elution of unwanted materials, the latter being crucial especially regarding elastomers and plastics, but also as regards silicone oil coatings e.g. on stoppers and syringes. If the packaging material manufacturer changes quality attributes of packaging components in contact with product, this forces the drug product manufacturer to prove safety and comparability which is not only costly but also time intensive. Finally, also the biopharmaceutical industry must think about avoidance of medicament counterfeiting, which does represent a large financial and safety concern not only in developing countries. One of the most advanced technologies in this field is RFID technology. In the seminar up-to-date packaging topics relevant for biopharmaceuticals will be exemplified by case stories. Input from regulatory bodies will be sought.

Moderators

Karoline B. Bechtold-Peters, Ph.D.
Boehringer Ingelheim Pharma GmbH & Co. KG

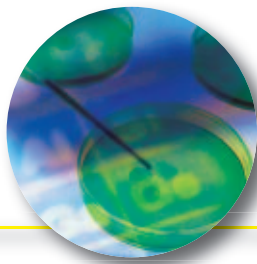
Adrienne L. Williams
West Pharmaceutical Services

Packaging Integrity—State-of-the-Art Testing Methods to Cope with the Risk-based Initiative

Markus Hemminger
Boehringer Ingelheim Pharma GmbH & Co. KG

The Challenge of Extractables and Leachables from Packaging Materials and Product-contacting Parts

Frances L. DeGrazio
West Pharmaceutical Services



Register now at:
www.aapspharmaceutica.com/nationalbiotech

Tuesday afternoon symposia
are funded by a grant from



1:00 pm - 3:30 pm
**Pharmacokinetic and
Pharmacodynamic Studies in
Assessing the Comparability of
Therapeutic Protein Products**
Symposium

Pharmacokinetic and pharmacodynamic (PK/PD) studies have generally been used for demonstration of bioequivalence between drug products with small molecules. These studies may also be found useful in the assessment of comparability of biopharmaceutical products with macromolecules such as therapeutic proteins. Under certain circumstances, PK/PD similarity may provide sufficient information in the evaluation of comparability of therapeutic protein products without the need for extensive clinical efficacy/safety data. This symposium will take a critical look at the application and analysis of PK/PD studies in establishing comparability of these products before and after manufacturing changes during the pre-approval and post-approval processes, as well as the role of PK/PD studies in developing follow-on protein products. Experts in the field will examine the advantages and limitations of using PK/PD studies for comparability assessment of therapeutic protein products. Case studies will be provided and regulatory applications will be discussed.

Moderator

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

**Utility of PK/PD Approach in
the Comparability Assessment
of Therapeutic Proteins—An
Academic Perspective**

Joseph Balthasar, Ph.D.
University at Buffalo

**Designing PK/PD Comparability
Studies for Registration of
Biosimilar Products**

Raja Velagapudi, Ph.D.
Barr Laboratories

**PK/PD Comparability of Therapeutic
Proteins—FDA Experience**

Hong Zhao, Ph.D.
U.S. Food and Drug Administration

**Special Considerations for PK/PD
Comparability Studies**

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

1:00 pm - 3:30 pm
**Exploratory IND (Phase 0 Trial)
and its Practices from
Biotechnology Perspectives**
Symposium

Optimizing exploratory drug development by means of doing first-in-human studies earlier is an attractive option for pharmaceutical developers to select more successful drug candidates. The regulatory authorities worldwide are getting increasingly concerned with paradigms that offer potential to accelerate patients' access to more optimized new drugs. In January 2003, the committee for proprietary medicinal products (CPMP) of the European Agency for the Evaluation of Medicinal Products (EMA) issued a position paper on the nonclinical safety studies to support clinical trials with a single microdose, which came into operation in July, 2003. In April, 2005, the U.S. Food and Drug Administration issued draft guidance for industry entitled 'Exploratory IND Studies.' This draft guidance emphasizes the concept that limited investigations in humans can be initiated with more limited preclinical support because such studies present fewer potential risks than do traditional phase 1 studies that look for dose-limiting toxicities. The draft guidance was finalized and became effective in January 2006. The new rules allow scientists to test sub-pharmacologic doses of a product, or doses expected to produce a pharmacologic, but not a toxic, effect, in limited human subjects within limited duration before full-scale clinical trials begin. The idea is to speed up drug development, and more importantly, to identify failing candidates and jettison them before costly clinical trials. The data from these early human studies could also help scientists design smarter trials for promising candidates. While the exploratory IND is being implemented, technical questions, comments and ethical concerns have been raised from various perspectives. This symposium will provide attendees with an overview of the exploratory IND, pros and cons found during the implementation period, the microdosing concept, and various challenges.

Moderator and Organizer

Lee Jia, Ph.D.
National Cancer Institute/NIH

**Human Phase 0 Microdose Studies—
Current Scientific and Regulatory
Perspectives**

Colin R. Garner, Ph.D., D.Sc.
Xceleron, Ltd.

**Strategies and Lessons Learned in
Implementing the Exploratory IND and
Phase 0 Clinical Trials at the NCI**

Joseph Tomaszewski, Ph.D.
National Cancer Institute/National Institutes
of Health

**Accelerating the Learning Phase of
Drug Development: The Value and
Limits of Novel Approaches to Early
Human Data Acquisition**

Liam Ratcliffe, M.D., Ph.D., MBA
Pfizer, Inc.

**Overview of Exploratory IND
(Phase 0 Trial): Differences
from the Traditional IND**

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

1:00 pm - 3:30 pm
**Aggregates of Proteins and
Their Conjugates: Detection,
Measurement, and Prevention**
Symposium

The significance of protein aggregation and misfolding as possible sources/causes of neurodegenerative diseases such as Parkinson's and Alzheimer's has been postulated for some time. Similarly, the effects of protein aggregation on the bioactivity of many, if not all, protein-based biologicals have been considered deleterious to the patient receiving such drugs. While further understanding of the causes of aggregation remains an area for active study and research, the knowledge that such aggregates are fraught with potential dangers has prompted the FDA in recent months to request that manufacturers focus on the need to eliminate their presence. Many of the methods commonly used over the intervening years to detect such aggregates often lacked the necessary sensitivity required. This was particularly evident for huge aggregates whose concentrations were far too small to detect by UV or other concentration detectors, yet whose immunogenic potential was often unparalleled. As there are so many areas for study of this so-called aggregation aggravation, this program will focus on but a few important facets of

—Continued on page 17

AAPS SUSTAINING SPONSOR

AAPS HONORS



*For Its support of the Association
During 2006-2007*

Pfizer Inc.

235 East 42nd Street
New York, NY 10017
www.pfizer.com



*Partnering To Build
The Pharmaceutical
Sciences*

AAPS SUSTAINING SPONSOR

AAPS HONORS



*For Its support of the Association
During 2006-2007*

Cardinal Health

14 Schoolhouse Road
Somerset, NJ 08873
Phone: (732) 537-6200
www.cardinal.com



*Partnering To Build
The Pharmaceutical
Sciences*

—Continued from page 14

the aggregation problem. These include measurements of the effects of formulation upon the creation of aggregates, aggregation artifacts caused by inappropriate analytical tools, determining the stoichiometry of protein aggregates with particular emphasis on hetero-associations and aggregates of conjugated proteins, means to reverse aggregation, and the high throughput screening of protein formulations.

Moderator

Philip J. Wyatt, Ph.D.
Wyatt Technology Corporation

Photodegradation and Aggregation of Proteins: Can We Prevent It?

Bruce Kerwin, Ph.D.
Amgen, Inc.

Stoichiometry of Aggregating/ Associating Conjugates

Michelle Chen, Ph.D.
Wyatt Technology Corporation

Huge Aggregates: Removing the Cloak of Invisibility

Donna Luisi, Ph.D.
Wyeth Biopharma

Interplay of Colloidal and Conformational Stability During Pressure-assisted Protein Disaggregation Processes

Theodore Randolph, Ph.D.
University of Colorado

Consequences of Aggregates in Biological Therapeutics

Amy Rosenberg, M.D.
U.S. Food and Drug Administration

1:00 pm - 3:30 pm Current Strategies for Pre-formulation and Formulation Development of Biopharmaceutical Products

Symposium

Approximately 50 percent of the investigational drugs in the pipeline are in the discovery and pre-clinical phases - that's over 10,000 molecules per Infinita's Report published in July 2006. Hence, pharmaceutical scientists, biochemists, and analytical chemists must manage a growing workload while designing products around the inherent complexities of large molecules. Externally, the expectations of an aging population require bringing new molecules to market faster, maintaining high

quality standards, meeting shelf-life requirements, improving safety, minimizing side effects and reducing the cost of drugs. Speakers for this symposium will provide strategies for preformulation and formulation development, and discuss in more detail problems that are faced by the scientists in the pre-formulation and formulation areas including identifying and overcoming low protein solubility, self-association, and offering advice for formulating high protein concentration products.

Moderators

Alisa K. Wright, MS
BioConvergence LLC

Sandeep S. Nema, Ph.D.
Pfizer, Inc.

Role of Self-association of Peptibody in Mediating Solution Instability

Yatin Gokarn, Ph.D.
Amgen, Inc.

Application of High-frequency Rheology Measurements in Analyzing Protein-protein Interactions in High Protein Concentration Solutions

Devendra Kalonia, Ph.D.
University of Connecticut

Pre-formulation Development Strategies for BioPharmaceutical Products

Frank Bedu-Addo, Ph.D.
IDD Consulting, LLC

Protein Solubility and Solubilization

Mitra Mosharraf, Ph.D.
HTD Biosystems, Inc.

Formulation Development Strategies for Biopharmaceutical Products

Jeff J. Schwegman, Ph.D.
BioConvergence LLC

1:00 pm – 6:30 pm Contributed Papers Session II

Authors will be present at their boards from 5:00 pm – 6:00 pm

3:30 pm - 5:00 pm Fill and Finish Process Development and Transfer to Commercial Manufacturing

Roundtable

Each product (planned for commercial manufacturing) needs to be transferred from R&D scale to commercial manufacturing

scale. This requires, already in an early stage, a precise project planning, a competent project team, a sophisticated application system and a filing strategy in order to meet the time to market approach. As an example, a freeze dried double chamber system introduced in clinical phase III and the transfer of the project to a 3rd party manufacturer will be shown. The different planning steps and milestones in regard to key-questions, conditions, results and further actions will be discussed.

Fill and Finish Process Development and Transfer to Commercial Manufacturing

Claudia Roth
Vetter Pharma-Fertigung GmbH & Co. KG

3:30 pm - 5:00 pm High Throughput Methods for Lead Discovery

Roundtable

High throughput methods of lead identification remain of interest to pharmaceutical scientists involved in all phases of discovery & development. High throughput screening has identified a variety of ligands for a number of target proteins. This program will update the audience on the NIH Molecular Libraries Roadmap Initiative, discuss applications leading to viable lead compounds and requirements for validation of HTS assays.

Moderator

Robert L. Chapman, Ph.D.
Midwestern University Chicago College of Pharmacy

NIH Molecular Libraries Roadmap Initiative

Christopher P. Austin, M.D. (*invited*)
National Institutes of Health

Validation of HTS Assays

Ajai K. Chaudhary (*invited*)
Eli Lilly and Company

Automation of Live Virus Vaccine Plaque Assay

Amy Keegan
Merck and Co.



Join AAPS –
Your Formula
for Success

TUESDAY & WEDNESDAY

3:30 pm - 5:00 pm

Data Analysis for Anti-product Antibody Assessment

Roundtable

This is a Part II of the discussion that took place at the NBC 2006 meeting. Immunogenicity is recognized widely as an important safety concern for the development of biopharmaceuticals. To date, it has not been possible to predict whether the generation of anti-drug antibodies will be inconsequential or have serious clinical consequences. For this reason and because the immunogenic potential of a biopharmaceutical can only be assessed in human studies, emphasis has been placed on optimizing assays for the detection of antibodies. Quasi-quantitative nature of anti-drug antibody assays and the unique features of the commonly employed assay formats have given rise to questions about what are the appropriate method validation and statistical analysis procedures for anti-drug antibody assays. Some important analytical performance characteristics for method validation where statistical considerations are pertinent include characterization of the sources of variability, assessment of sensitivity, estimation of imprecision, and evaluation of titer reproducibility. Such issues as statistical estimation of a method's 'cut-point' and normalization factor and other will be discussed. Discussion will also focus around greater harmonization of method development approaches within the pharmaceutical and biotechnology industry. This session will share common issues and problems seen in the analysis anti-drug antibody validation data and offer recommendations for statistical approaches.



AAPS Members enjoy significant savings at the 2007 AAPS National Biotechnology Conference.

Moderators

Boris M. Gorovits, Ph.D.
Wyeth

Ronald R. Bowsher, Ph.D.
B2S Consulting LLC, and
LINCO Diagnostic Services, Inc.
... a Millipore Company

Practical Consideration for Using the Results of Statistical Evaluation of Immunogenicity Assays

Bonita Rup, Ph.D.
Wyeth

Title to be Announced

Viswanath Devanarayan, Ph.D.
Merck Research Laboratories

Title to be Announced

Wendell Smith, Ph.D.
Bowsher Brunnelle Smith, LLC

3:30 pm - 5:00pm

TGN1412

HOT TOPIC

Description, Titles, Speakers to be Announced

5:00 pm - 6:30 pm

Cocktail Reception

Wednesday, June 27

7:00 am - 5:00 pm

Registration

9:30 am - 1:00 pm

Career Center

9:30 am - 1:00 pm

Exhibits

9:30 am - 1:00 pm

Contributed Papers Session II
Conclusion

7:30 am - 8:30 am

Intracellular Trafficking and Processing of Macromolecules

Sunrise Session

We will provide the audience an insight into the events and processing pathways regulating the movement of therapeutic macromolecules from extracellular environment to their target site in the cell. Modern drug delivery strategies are increasingly focused on delivering the drugs to their target location in the cell. Efficient intracellular delivery of macromolecular drug candidates requires an understanding of the major barriers that limit the cellular entry of macromolecules, endocytic pathways that control their intracellular movement, factors that regulate the release of macromolecules from the endosome, and agents that manipulate or perturb these pathways. The advent of cellular imaging techniques have brought us closer to appreciate these intricate events which control the intracellular fate of proteins, lipids and nucleic acids. This sunrise session is therefore designed to provide the audience an understanding of the events and cellular factors that could limit or promote the interaction of therapeutic macromolecules to their intracellular targets, thus controlling drug activity. The intended audience for this session includes scientists from both the academia and industry affiliated with the BIOTEC, CS, PDD, and PPDM sections, besides graduate students and trainees in pharmaceutical sciences.

Moderator

Arvind K. Chappa, Ph.D.
The University of Kansas

Title to be Announced

Jeff Krise, Ph.D.
The University of Kansas

Title to be Announced

Kyung-Dall Lee, Ph.D.
The University of Kansas

7:30 am - 8:30 am

Production and Qualification of Positive Controls for Neutralizing Antibody Assays

Sunrise Session

Neutralizing antibodies developed during the course of therapeutic biologics have implications on PK/safety/efficacy. Concentration of neutralizing antibodies are

often presented in relative concentration to a reference antibody. This session covers topics such as selection of animal species, techniques of producing the reference antibody, qualification and release specification of the antibody, proper handling and utility of antibodies during assay development, and proper interpretation of assay results (quantitative or semi-quantitative).

Moderators

Lakshmi Amaravadi, Ph.D.
BiogenIdec

Lynne Lesauteur, Ph.D.
Charles River Laboratories

Generation and Characterization of Positive Controls for Neutralizing Antibody Assays

Denise M. O'Hara, Ph.D.
Wyeth Research

Qualifying Positive Controls for Neutralizing Antibody Assays

Sue Richards, Ph.D.
Genzyme Corporation

7:30 am - 8:30 am Monoclonal Antibodies PK/PD First Principles

Sunrise Session

Monoclonal antibodies represent one of the fastest growing areas of new drug development within the pharmaceutical industry. With both large, established biotechnology companies and small start-ups involved in the development of this important class of molecules, monoclonal antibody products will become increasingly prevalent over the next decade. Although monoclonal antibodies (mAbs) constitute a major advance in therapeutics, their pharmacokinetic (PK) and pharmacodynamic (PD) properties are not fully understood. It is widely accepted that the binding of mAbs to their target antigen explains part of their nonlinear PK/PD properties. Recently, the appropriateness of the classically used Langmuir or Michaelis-Menten characterization of mAb binding to the target ligand has been challenged in favor of fundamental second order binding equations initially popularized by Gaddum because of the similar molar ranges of mAb dose and target ligand. This sunrise session will provide attendees with an understanding of how examining PK simultaneously with PD of the target ligand allows explanation of observed non-linearities and permits the determination of the kinetics of free mAb, ligand and complex.

Moderator

David Lau, Ph.D.
Johnson & Johnson

Building mAb PK/PD Models from First Principles

Philip Lowe, Ph.D.
Novartis

Binding to the Target Ligand: PK/PD of Monoclonal Antibodies Unveiled

Donald Mager, Ph.D.
University at Buffalo, SUNY

9:00 am - 11:30 am Quality by Design and Risk Management in Biologics Process Development and Manufacturing

Symposium

This symposium will address industry and regulatory trends in the process development and manufacturing of biologics, particularly focusing on the application of design space and risk management approaches. The presentations will include discussion of practical tools and process analytical technologies, along with regulatory considerations. The speaker panel will include industry and regulatory representatives, and will discuss case studies or examples to illustrate progress and challenges in the real-life application of Quality by Design and Risk Management concepts presented in recent guidances (e.g., ICH Q8 and Q9).

Moderators

Manpreet-Vick S. Wadhwa, Ph.D.
Amgen, Inc.

Satish K. Singh, Ph.D.
Pfizer, Inc.

Statistical and Analytical Tools to Define Design Space and Evaluate Risk

Clarice J. Hutchens, Ph.D.
Pfizer, Inc.

Applying QbD and Risk Management to Biotech Manufacturing - Role of PAT

Harry Lam, Ph.D.
Genentech, Inc.

Incorporating Risk Management into QbD from a Biotechnology Product Quality Perspective

Anthony Mire-Sluis, Ph.D.
Amgen, Inc.

Recommendations for Achieving the Desired State in QbD and Risk Management

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

9:00 am - 11:30 am Chemical and Physical Stability of Therapeutic Antibodies

Symposium

Recombinant monoclonal antibodies (Mab) are an emerging therapy for a variety of diseases. The field is rapidly expanding and will fuel the Biotech and increasingly large Pharma industry for years to come. The number of molecules in development combined with the ever increasing sophistication of analytical characterization technologies has increased the scrutiny put on characterizing chemical and physical properties of these proteins during processing, storage, and delivery. This symposium will highlight novel analytical approaches to identify common and not-so-common chemical modifications and discuss the characterization of solution behaviors of antibody under high concentrations. The symposium will offer insights into mechanisms of chemical degradation pathways in antibody as well as underlying physical parameters impacting solution behavior. In addition, topics on optimizing stability by means of formulation and antibody engineering will also be discussed.

Moderators

Wolfgang Glaesner, Ph.D.
Eli Lilly and Company

Jirong Lu, Ph.D.
Eli Lilly and Company

Characterization of Phase Separation Behaviors of Antibodies

Kent Amsberry, Ph.D.
Eli Lilly and Company

Measurement of Net Charge and Its Role on Solution Behaviors of Antibody

Thomas Laue, Ph.D.
University of New Hampshire

The Antibody Toolbox: Characterization of Chemical Heterogeneity of Intact Monoclonal Antibodies

Gerd Kleemann, Ph.D.
Amgen, Inc.

WEDNESDAY

Provisional: Biophysical Properties of Human Antibody Variable Domains

Andreas Plueckthun Ph.D., *(invited)*

University of Zurich

FDA Perspective on Protein Aggregation

Amy Rosenberg, M.D.

U.S. Food and Drug Administration

9:00 am - 11:30 am

Novel Vaccine Delivery Systems: Application to Human and Animal Health

Symposium

Most vaccines are delivered by injection using syringes and needles, which have several shortcomings such as needle-stick injuries, risk of transmission of diseases, difficulties in mass immunization, etc. Health organizations are beginning to look for safer alternatives that reduce the risk of cross-contamination and increase convenience to, and compliance by, the users. Not surprisingly, the development of needle-free immunization methods has now been identified as an important goal in global health care industry. Current methods of needle-free immunization, either commercially available or under development, can be classified into two broad classes: mucosal immunization (oral, nasal and respiratory), and cutaneous immunization, depending on the site of vaccine administration. In the past decade there has been significant progress in addressing the technological challenges that are associated with immunization without needles by oral, nasal/inhalation and cutaneous routes. The presentations in this symposium focus on contemporary developments in novel vaccine delivery systems by transmucosal and transcutaneous routes and their applications to humans and animals.

Moderators

Hye-ok H. Choi, Ph.D.

3M

Julie D. Suman, Ph.D.

Next Breath LLC

Novel Adjuvants for Mucosal Vaccine Delivery

Paul Dominowski, Ph.D.

Pfizer Animal Health

FDA Regulations for Biologic Products and Vaccines

Ellen Flannery

Covington & Burling

Transcutaneous Immunization: Considerations for Qualifying a New Combination Vaccine Product

John K. Simons, Ph.D.

3M

Needle-free Immunization Technologies—Overview

Samir Mitragotri, Ph.D.

University of California, Santa Barbara

Inhalation Vaccines and Immunological Challenges

David A. Edwards, Ph.D.

Harvard University

9:00 am - 11:30 am

Preformulation Challenges and Processing Approaches to Biologic Product Development

Symposium

This symposium will focus on the issues of protein stability, specifically aggregation phenomena, and also processing approaches to overcome these challenges. Aggregation is a common problem that needs to be identified during early development of biological proteins and must be addressed for many dosing routes, for example high concentration injections and solid dosage forms. The biggest challenge of controlling aggregation is its complex mechanism of formation and nonlinear progression. Emerging science is the utilization of computational methodologies to predict aggregation, and the resulting immunogenicity issues. Lyophilization is the current method of choice for formulation and processing of biological molecules into the stabilized dry powders. Spray-freeze drying (SFD) is relatively new but rapidly growing field which may become a viable economical alternative to both the standard lyophilization and spray-drying, often providing a superior product by means of particle engineering. Some of these novel processing methods will be discussed.

Moderators

Matthew J. Mollan, Ph.D.

Pfizer, Inc.

Boris Y. Shekunov, Ph.D.

Ferro Pfansteihl Laboratories

Modeling and Predicting Protein Aggregation: What Have We Learned, and What Are We Missing?

Christopher Roberts, Ph.D.

University of Delaware

Recent Advances in Processing of Biologicals

Speaker to be Announced

Spray Freeze Drying to Produce Stable Formulations of Adjuvanted Subunit Vaccines

Theodore Randolph, Ph.D.

University of Colorado

Early Stage Protein Formulation Development and Use of High Throughput Screening Methods

Tapan Das, Ph.D.

Pfizer, Inc.

9:00 am - 10:30 am

Immunogenicity: Science and Regulatory Perspectives

Roundtable

Immunogenicity is quite unique to large biological molecules. Biopharmaceutical industry and government agencies are facing many challenges in this field. What are the impact of immunogenicity on the safety and efficacies in human of the biological drug products? How and when can/should immunogenicity be detected and monitored? Are current scientific methods and models sufficient and adequate to detect and measure differences in immunogenicity of biotech products manufactured by different sponsors/sites? How can these methodologies and models be used in the development of biotech products? What are the review standards and submission requirements on immunogenicity? Is post-marketing surveillance required? What are the regulatory requirements and expectations by the U.S. FDA on immunogenicity from development to post marketing approval? How is the similarity of biotech products produced by different manufacturers evaluated from the immunological perspective? This roundtable session is intended to discuss the recent development of scientific knowledge, methodology and regulatory requirements in immunogenicity and potential solutions to the challenges.

Moderator

Xiaomi M. Tong, Ph.D.

Emergent BioSolutions, Inc.

The Incidence and Prevalence of Neutralizing Inhibitors in Previously Treated and Previously Untreated Hemophilia A Patients: The Role of Product Class or Specific Product

Jay Feingold
Wyeth

Title to be Announced

Amy Rosenberg, M.D.
U.S. Food and Drug Administration

9:00 am - 10:30 am

Scale-up, Technology Transfer, and Process Validation During Biologics Development

Roundtable

Process validation is essential to the production of quality biotech products. Process changes can impact product identity and quality. However, multiple changes and scale-up can occur during product development. How can we ensure the product is comparable after changes have been made? Furthermore, validation requires resources and time. To wisely allocate the resources at appropriate time during development, decisions have to be made on what processes and parameters, at what time, and on which product candidates validation needs to be conducted. Frequently, a firm needs to transfer technology between different groups, sites and sometimes to a different firm. How product quality can be guaranteed after technology transfer? What principles and what processes should apply to a tech transfer? This session is devoted to discussion of issues, approaches, regulations and science related to scale-up, technology transfer, and validation in the drug development.

Moderator

Jim Li, Ph.D.
Wyeth

Title to be Announced

Patricia Hughes Troost, Ph.D.
U.S. Food and Drug Administration

Title to be Announced

Xiaomi M. Tong, Ph.D.
Emergent BioSolutions, Inc.

9:00 am - 10:30 am

Analysis of the Nature of Assay Interferences

Roundtable

Ligand binding assays are prone to various assay interferences. The main cause of such interferences is generally due to interaction of matrix components with assay reagents. This roundtable will focus on various methods and approaches that can be used to identify interfering components and to reduce matrix-related problems. For example, proteomics approaches used to identify specific interferences will be discussed. Possible impact on the pharmacokinetic analysis in cases where interference is observed will be discussed.

Moderator

Boris M. Gorovits, Ph.D.
Wyeth

Title to be Announced

Michel G. Awwad
Wyeth

Title to be Announced

Deborah L. Finco-Kent
Pfizer

Proteomics Approaches to Identify Specific Interferences Case: Studies

Boris M. Gorovits, Ph.D.
Wyeth

11:30 am - 1:00 pm

Graduate Student Symposium

Funded by a Grant from



1:00 pm - 3:30 pm

Designing the Next Generation of Therapeutic Antibodies

Symposium

Recombinant monoclonal antibodies have become a common tool for the treatment of widespread diseases like cancer, inflammatory diseases, asthma, and multiple sclerosis. The engineering of antibodies has initially been focused on variable regions to generate tight binders with high specificity and selectivity. Significant scientific innovation has been achieved over recent years to achieve this goal, using a variety of different approaches and technologies. More recently, significant emphasis has been put on improving the potency of antibody therapies by engineering properties of its constant regions. This symposium provides an overview of state-of-the-art strategies for antibody engineering and discusses how further engineering can improve the clinical performance of monoclonal antibody therapies.

Moderators

Andrew M. Vick, Ph.D.
Eli Lilly and Company

Wolfgang Glaesner, Ph.D.
Eli Lilly and Company

The Protein Engineering Approach to Enhance Antibody Effector Function: A Case Study

Mary-Ann Campbell, Ph.D.
Applied Molecular Evolution

Provisional: Enhancing Antibody Effector Functions Through Glycoengineering

Pablo Umana, Ph.D.
Glycart Biotechnology

Provisional: Increasing Antibody Half-life Via Engineering FcRN Interactions

Richard Murray, Ph.D.
PDL Biopharma

Superantibodies

Heinz Kohler, Ph.D., M.D.
InNexus Biotechnology, Inc.

Multifunctional Antibodies by the Dock-and-Lock Method of Designer Fusion Proteins for Improved Cancer Therapy

David Goldenberg, Sc.D., M.D.
Immunomedics, Inc.

1:00 pm - 3:30 pm

Immunogenicity: Approaches to Improving the Detection of Antibodies to Biological Therapeutics in Samples Containing Drug

Symposium

Therapeutic proteins have the potential to generate anti-drug antibodies that may impact both safety and efficacy of the protein therapeutic. It is important to develop and validate assays to detect anti-drug antibodies, however the presence of drug in patient samples can affect the ability of an assay to detect antibodies. Ideally, washout samples would be evaluated, however this is not always possible especially in studies using frequent and high level dosing regimens. Thus, methods to remove drug and/or improve detection of antibodies in the presence of drug are needed. This symposium will present discussion on the state of the art approaches to improving detection of antibodies to biological therapeutics in the presence of drug. Speakers will present case studies utilizing various approaches to addressing this problem.

Moderator

Deborah L. Finco-Kent
Pfizer, Inc.

Sample Pretreatment Method Followed by ECL Analysis: A Case Study for Drug Removal

Deborah L. Finco-Kent
Pfizer, Inc.

Improving Immunogenicity Assay Tolerance to Interfering Substances

Mike Moxness, Ph.D.
Amgen, Inc.

Development and Validation of a Drug Tolerant ELISA for Determination of Antibodies to a Human Therapeutic Antibody

Holly Smith
Eli Lilly and Company

Immunogenicity Testing by Quantitative Mass Spectrometry: Overcoming the Interference of Excess Protein Therapeutics

Hendrik Neubert
Pfizer, Inc.

1:00 pm - 3:30 pm Macromolecular Microdialysis

Symposium

This symposium will highlight methodological advances and emerging applications of microdialysis technology as applied to cytokines, chemokines, growth factors and neuropeptides. To date, microdialysis has been perceived primarily as a technology for sampling and local delivery of small molecules, since most applications have concerned solutes with molecular weights under 1 kDa. However, commercial probes are available with membranes of 100 kDa molecular weight cutoff membranes. Furthermore, users can construct probes of even higher cutoffs with hollow fiber membranes produced for microfiltration purposes, such as plasmapheresis. Consequently, microdialysis is now feasible for large biomolecules, such as polypeptides and proteins. Opportunities for exploiting macromolecular microdialysis exist at many levels: basic research, diagnosis, clinical monitoring and manufacturing process control. This capability is highly relevant to the programming of the AAPS National Biotechnology Conference (NBC), which generally relates more to higher molecular weight agents, such as protein biologics, than the programming of the AAPS Annual Meeting.

Whereas, microdialysis has been the subject of numerous sessions at past Annual Meetings, the technology has not here-to-fore been highlighted at NBC. This symposium brings together some of the foremost practitioners to realistically appraise the capabilities of microdialysis for an important subset of macromolecular biomolecules, namely the cytokines, chemokines, growth factors and neuropeptides. These agents are of interest because of their role as endogenous regulatory and signaling agents, as well as for their use as therapeutics.

Moderators

Peter M. Bungay, Ph.D.
National Institutes of Health

Julie A. Stenken, Ph.D.
Rensselaer Polytechnic Institute

Use of Large Pore Membranes and Multiplex ELISA Kits in Inflammatory Response Studies

Martin Schmelz, M.D.
University of Heidelberg

Microdialysis of Growth Factors in Breast Cancer

Charlotta Dabrosin, M.D., Ph.D.
University Hospital Linköping

Ultramicro Analytical Techniques

Terry M. Phillips, Ph.D.
National Institutes of Health

Microdialysis of Large Molecules

Geraldine F. Clough, Ph.D.
University of Southampton

1:00 pm - 3:30 pm Novel Approaches to Extravascular Delivery of Peptides and Proteins

Symposium

Traditionally, peptides and proteins are delivered via parenteral routes, such as intravenous, subcutaneous, and intramuscular injections. In recent years, novel technologies have been applied to delivery of these molecules, in order to improve the dosing convenience and patient compliance. The objective of this symposium is to provide an update on the recent development of novel technologies for extravascular delivery of peptides and proteins. Technologies including inhalation, intranasal, transdermal, and oral administration will be discussed.

Topics that will be covered during each presentation include overview of the technology, proof-of-concept, evaluation of the suitability of each technology for different molecules, as well as issues in product development, clinical testing, and commercialization.

Moderator

David Lau, Ph.D.
Johnson and Johnson

Intranasal Delivery Bypasses the Blood-brain Barrier to Target Drugs to the CNS and Reduce Systemic Exposure

William H. Frey II, Ph.D.
University of Minnesota

Inhalation Delivery of Peptides and Proteins

John Patton, Ph.D.
Nektar Therapeutics

Oral Delivery of Macromolecular Therapeutics from Discovery to Product Development

Steven Dinh, Sc.D.
Emisphere Technologies, Inc.

Electrotransport of Large Molecules Through the Skin

Michel Cormier, Ph.D.
Alza Corporation

3:30 pm - 5:00 pm Immunogenicity and Correlations with Clinical Data

Roundtable

This session will describe data that helps define the clinical consequences of immunogenicity. There are many examples where antibodies are formed against protein therapeutics and yet there are no clinical consequences. Unfortunately, there have been a few instances where the immune response to a protein therapeutic has had significant clinical consequences for the patient. This session will discuss some of the risk factors that can help us understand the clinical implications of an immune response to a protein therapeutic.

Neutralizing Antibody Development and Class Switching in Clinical Patients with Idiopathic Parkinson's Receiving r-metHuGDNF Via Intrapataminal Infusion

Mike Moxness, Ph.D.
Amgen, Inc.

Evaluating the Impact of Immunogenicity on Pharmacological Activity, Efficacy, and Safety in Naglazyme™ Clinical Trials

Joleen T. White, Ph.D.

BioMarin Pharmaceutical, Inc.

Immunogenicity in a Clinical Context: Therapeutic Monoclonal Antibodies

Valerie E. Quarmby, Ph.D.

Genentech, Inc.

3:30 pm - 5:00 pm

Novel and Conventional Reagents Used in Ligand Binding Assays

Roundtable

Presentations will discuss case studies of approaches related to managing conventional critical reagents and the emerging use of novel reagents for ligand binding assays. To generate high quality ligand binding assays, accurate assay data and therefore make the best decisions at all phases of drug development, good assay reagents are required in adequate quantities and with established supply chains. During different phases of the drug development pipeline varying quality, quantities and characterization of reagents are necessary. So that appropriate deployment of resources is vital to the continuous supply, technology transfer and characterization of critical reagents that support biopharmaceutical development activities. As increasing demand is placed on drug development pipeline deliverables and drug advancement, more diverse groups are using these ever increasing numbers of ligand binding assay critical reagents. Discussions will focus on approaches taken to create highly efficient, managed systems that are maintained and supplied with well-characterized critical reagents. Case histories will describe problem-solving strategies. Traditionally reagents used in ligand binding assays are proteins of various sizes and affinity, which include monoclonal and polyclonal antibodies, receptors, ligands, peptides and other binding proteins. Novel non-protein reagents are emerging in bioanalytical assays. Some of these novel reagents include nucleic acid aptomers, RNA and DNA as well as quantum dots as dyes. Long-term stability, supply chain and reproducibility of reagent lots are all of concern to the assay developer and validating lab and will be discussed.

Moderator

Denise M. O'Hara, Ph.D.

Wyeth

What's So Critical About Reagents? Their Effective Characterization and Management for Ligand Binding Assays

Denise M. O'Hara, Ph.D.

Wyeth

Novel Reagents for Use in Bioanalytical Assays

Speaker to be Announced

3:30 pm - 5:00 pm

Statistical Analysis of Results of Ligand Binding Assay as Applied to PK Interpretation

Hot Topic

During the 2006 AAPS Workshop on Bioanalytical Methods Validation, a considerable amount of discussion was focused on statistics as applied to LBA protocols and then utilized to calculate PK parameters. It was agreed that more discussions are needed in relationship to the following areas: total error application; 4-6-20 rule versus 4-6-30 rule; the impact on PK analysis and interpretation as a result of the level of variability observed in the assay including possible non-parallelism; various stability related issues and repeat measurement of incurred samples. Analytical and PK scientists, as well as statisticians will be invited to make presentations at this session.

Moderator

Boris M. Gorovits, Ph.D.

Wyeth Research

Title to be Announced

Jean Lee, Ph.D.

Amgen, Inc.

Title to be Announced

Bruno Boulanger, Ph.D.

Eli Lilly and Company

Parallelism Analysis Case Study

Boris M. Gorovits, Ph.D.

Wyeth Research

3:30 pm - 5:00 pm

Delivering Macromolecules by Nebulization—From Proof of Concept to Commercialization

Roundtable

New chemical entities targeted for pulmonary administration often enter proof-of-concept studies or Phase I human studies delivered by nebulizers. Then, as the product advances through clinical trials, it is converted to an alternative delivery system. The focus of this symposium is to understand nebulizer standards, formulation development and scale-up issues related to delivery of large molecules by nebulizers. In addition, bridging studies and strategies for Phase II/III studies for selection of the final delivery system will be discussed.

Moderator

Michael Riebe, Ph.D.

Merck and Company, Inc.

Case Study—Getting to Phase I

Stefan Seemann (*invited*)

Pari

Case Study—Making the Conversion

Ralph Niven, Ph.D.

Innoven

Converting Device Platforms - A CMC Planning Overview

Elaine Phillips, Ph.D., (*invited*)

Verus Pharmaceuticals

Attention Authors

Are you planning to submit your research for publication?

Support AAPS' premier journals by sending your papers to

The AAPSJournal™ OR **AAPS PharmSciTech™**



For more information go to:

www.aapsj.org OR www.AAPSPHARMSCITECH.org

The aaps
Journal

aaps
PharmSciTech™