Cambridge Healthtech Institute’s Sixth Annual

Immunogenicity and Bioassay Summit 2014

Technologies and Strategies for Safe and Efficacious Products in the Clinic

Attend the Number 1 Immunogenicity and Bioassay Event Bringing Together Industry, Academia and Regulatory Authorities

November 17 - 18

Immunogenicity Assessment & Clinical Relevance

Keynote Speakers

Steven J. Swanson, Ph.D.
Executive Director, Medical Sciences, Clinical Immunology, Amgen, Inc.

Amy Rosenberg, Ph.D.
Director, Therapeutic Proteins, FDA/CDER

Baolin Zhang, Ph.D.
Senior Investigator, Therapeutic Proteins, Biotechnology Products, FDA

Jaya Goyal, Ph.D.,
Director, Translational Sciences, Biogen Idec

November 18 - 19

Immunogenicity Prediction & Mitigation

Optimizing Bioassays for Biologics

Join Over 250 of Your Peers!
What’s NEW for 2014?

- Eight FDA presenters this year
- More on immunogenicity challenges in clinical development: pre-existing reactivity, target interference, Fc-Fc interactions, drug interference, impact of higher order complexes, characterization of ADAs, assay validation and cut points
- Focus on specific products: interferon beta, enzyme replacement therapy, Knob-and-Hole therapeutics, ADCs, Factor VIII, immunotoxins, hemophilia products, Adnectins
- Choice of 14+ new interactive breakouts for in-depth discussion
- More focus on the impact of sub-visible particles, aggregates and impurities
- New angle on impact of route of administration
- Increased coverage and case studies on feedback from health authorities
- Presentations on working with molecules with multiple mechanisms such as ADCs, bispecifics, and fragments

Sponsorship, Exhibit, and Lead Generation Opportunities

CHI offers comprehensive sponsorship packages which include presentation opportunities, exhibit space, branding and networking with specific prospects. Sponsorship allows you to achieve your objectives before, during, and long after the event. Any sponsorship can be customized to meet your company’s needs and budget. Signing on early will allow you to maximize exposure to qualified decision-makers.

Podium Presentations – Available Within the Main Agenda!
Showcase your solutions to a guaranteed, targeted audience. Package includes a 15- or 30-minute podium presentation within the scientific agenda, exhibit space, on-site branding, access to cooperative marketing efforts by CHI, and more.

Breakfast & Luncheon Podium Presentations
Opportunity includes a 30-minute podium presentation. Boxed lunches are delivered into the main session room, which guarantees audience attendance and participation. A limited number of presentations are available for sponsorship and they will sell out quickly. Sign on early to secure your talk!

Invitation-Only VIP Dinner/Hospitality Suite
Sponsors will select their top prospects from the conference pre-registration list for an evening of networking at the hotel or at a choice local venue. CHI will extend invitations and deliver prospects, helping you to make the most out of this invaluable opportunity. Evening will be customized according to sponsor’s objectives i.e.:• Purely social
• Focus group
• Reception style
• Plated dinner with specific conversation focus

Exhibit
Exhibitors will enjoy facilitated networking opportunities with qualified delegates. Speak face-to-face with prospective clients and showcase your latest product, service, or solution.

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CHI’s Lead Generation Programs will help you obtain more targeted, quality leads throughout the year. We will mine our database of 800,000+ life science professionals to your specific needs. We guarantee a minimum of 100 leads per program! Opportunities include:

- Whitepapers
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Additional branding and promotional opportunities are available, including:

Advertising opportunities such as marketing and promotional emails are also available.

For sponsorship and exhibit information, please contact:
Carolyn Benton
Business Development Manager
781-972-5412 | cbenton@healthtech.com
**Short Courses**

**SUNDAY, NOVEMBER 16**

1:30 – 4:30 pm SC1: Basics of Immunogenicity Testing  
Instructors:  
Jim McNally, Ph.D., Senior Principal Scientist, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

This interactive session will enable attendees to work out a basic immunogenicity preclinical and clinical testing strategy for various molecules including bi-functional and other novel scaffolds. Areas of difficulty will be discussed with specific case studies. Attendees are encouraged to contribute with their own experiences and to bring questions for discussion or submit to the meeting organizers in advance.

The following topics will be covered:
- Basic issues regarding screening, confirmatory and titer assays
- Assay methodologies and various technologies
- Current approaches to data analysis and cutoffs
- Preclinical and clinical considerations
- Common problems

5:30 – 8:30 pm Dinner SC2: Challenges of Immunogenicity Assessment  
Instructors:  
Jim McNally, Ph.D., Senior Principal Scientist, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

This interactive session of intermediate level will focus on the potential challenges of immunogenicity testing in preclinical and clinical development and present case studies demonstrating how they can be handled. Attendees are encouraged to contribute with their own experiences and to bring questions for discussion or submit to the meeting organizers in advance.

The following topics will be covered:
- Challenges and approaches to resolve commonly encountered issues
- Multi-domain binding proteins
- Pre-existing ADAs
- Emerging trends in the development of neutralizing antibody assays
- Cross-reactivity to endogenous proteins
- Clinical implications of ADAs

**TUESDAY, NOVEMBER 18**

6:30 – 9:30 pm Dinner SC3: Immunogenicity Risk Assessment and Regulatory Strategy  
Instructors:  
Laurie Graham, Ph.D., Product Quality Reviewer, Division of Monoclonal Antibodies FDA/CDER  
Bridget Heelan, MB, Ph.D., Vice President, Consulting, Parexel (ex-MHRA)

Priorities for the regulator:  
Hierarchy of concerns; Data requirements; Common gaps

Integrated approach:  
Risk identification; Aligning identified risks with CMC; Bioanalytical, non-clinical and clinical strategy; Ongoing risk management

Difficulties in comparative immunogenicity assessment:  
One versus two assay format for comparing biosimilars to innovators

Interactive case study:  
Illustration of preparation of an effective response to a regulatory scenario pertaining to immunogenicity-related risks for an investigational therapeutic protein

Questions and Answers

The following topics will be covered:
- Benefits of timely discussion with the regulators
- Neutralizing antibody assays (NAbs): When are they necessary?
- The case for binding assays versus cell-based assays for NAbs
- Novel products and biosimilars: What challenges are the regulatory authorities seeing and anticipating?
- Pitfalls to avoid

6:30 – 9:30 pm Dinner SC4: Strategic Bioassay Design and Analysis  
Instructor:  
Liming Shi, MS, MA, Senior Research Scientist, Bioassay Development, Eli Lilly & Company

This course will focus on the fundamentals of statistics and simple methodology that are routinely applied in the bioassay laboratory. Covered topics will include a review of statistical concepts and calculations, study design, assessing bioassay measurement quality and comparative studies.

The following topics will be covered:
- Uniqueness of bioassay, especially cell-based potency assay
- Considerations in bioassay development and validation
- Bioassay measurements and calculations
- Quality control of bioassay performance
- Comparative studies for bioassay development and transfer
MONDAY, NOVEMBER 17

7:30 am Registration and Morning Coffee

8:30 Chairperson’s Opening Remarks

Steven J. Swanson, Ph.D., Executive Director, Medical Sciences, Clinical Immunology, Amgen, Inc.

CHALLENGES WITH IMMUNOGENICITY ASSESSMENT

8:35 Cut Points and Confirmatory Assays: A Case Study of Pre-Existing Reactivity, ADCs and Statistics

Jim McNally, Ph.D., Senior Principal Scientist, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

Determination of cutpoints for screening and confirmatory assays is a straightforward process for normal, drug-naïve individuals with no baseline reactivity for the drug. However, with increasing frequency, pre-existing reactivity is observed in anti-drug antibody assays and these individuals complicate the process of setting the cutpoint. A case study will be presented where a large percentage of normal individuals exhibited pre-existing reactivity and describes the methods to determine an appropriate cutpoint.

9:05 Overcoming Challenges with Target Interference in ADA Assays: A Case Study in Multimeric Targets

Reza Mozaffari, Investigator, Clinical Immunology, GlaxoSmithKline

Multimeric targets present in clinical samples can cause interference in bridging assay formats used for anti-drug antibody (ADA) detection. This interference may potentially generate a false positive result which could impact the immunogenicity assessment of the compound. I will present our experiences and the different approaches we have used to minimize interference of this nature.

9:30 Minimizing Interference from Fc-Fc Interactions in Bridging Immunogenicity Assays for IgG4 Monoclonal Antibody Therapeutics

Michael Partridge, Ph.D., Staff Scientist, Bioanalytical Sciences, Regeneron Pharmaceuticals, Inc.

Human IgG4 antibodies are known to interact with other IgG4s via their Fc. In bridging immunogenicity assays, IgG4 Fc-Fc contacts generate increasing signal over time for the negative control, reducing assay sensitivity and complicating confirmation cut point determination. Increasing background signal over time is especially problematic for automated analysis, as reagents are prepared in advance and used over several hours during a run. This presentation will discuss these interactions and the impact they have on immunogenicity assays for IgG4 drugs.

10:05 Overcoming the Challenges of Immunogenicity and Cell Based Neutralizing Antibody Assays for Biosimilar Drug Development

Kathryn Lindley, M.S., Director, Bioanalytical Operations, BioAgilitytix Labs

Successful development of biosimilar drugs requires demonstration of biosimilarity to the originator drug. Immunogenicity assays require extensive method development and validation to support preclinical and clinical comparative studies, and overcoming the challenges of developing cell based assays to detect neutralizing antibodies is critical for success. The challenges of development and validation of qualitative immunogenicity (ADA) screening assays, and neutralization (Nab) assays for biosimilar drug development will be presented.

10:35 Coffee Break in the Exhibit Hall with Poster Viewing

NEUTRALIZING ANTIBODY ASSAYS AND MANAGING DRUG INTERFERENCE

11:15 Drug Interference and Other Challenges with the Development of Neutralizing Antibody Assays

Renuka C. Pillutla, Ph.D., Director, Bioanalytical Sciences – Biologics, Bristol Myers Squibb

Neutralizing antibody assays are inherently prone to interference from circulating drug in-vivo. This is a particular concern with therapeutic monoclonal antibodies due to long half-lives. To improve drug tolerance for the determination of human neutralizing antibodies in a competitive ligand-binding assay, Solid-Phase Extraction with Acid Dissociation (SPEAD) was implemented, which significantly increased the amount of tolerated drug in the assay.

11:45 Improving Drug Tolerance in a Clinical Neutralizing Antibody Assay by Solid-Phase Extraction with Acid Dissociation

Gisela Peraus, Ph.D., Lab Head, Pharmacology, Novartis Biologics

Neutralizing antibody assays are inherently prone to interference from circulating drug in-vivo. This is a particular concern with therapeutic monoclonal antibodies due to long half-lives. To improve drug tolerance for the determination of human neutralizing antibodies in a competitive ligand-binding assay, Solid-Phase Extraction with Acid Dissociation (SPEAD) was implemented, which significantly increased the amount of tolerated drug in the assay.

12:15 pm Immunogenicity of Topical Drug Products

Mirela Ionescu, Principal Scientist, Immunology, Charles River Montreal

Immunogenicity testing is a critical step in the development of biotherapeutics. Although topical dermatological products are typically lower in immunogenic potential, in some instances they do have the potential to induce an immunologic response. During this presentation, a case study where an anti-cancer antibody was administered topically in mini-pigs and humans will be discussed. A dose-dependent immunogenic effect was observed in both the preclinical and clinical studies, further confounding the need for early phase immunogenicity assessment of topical drug products and the clinical relevance of performing such assessments.
12:45 ImmunoCAP ADA Bridging Assay – A New ADA Assay with High Inter-Laboratory Precision Based on a IVD Platform

Camilla Eriksson, Senior Scientist, New Technology Development, Thermo Fisher Scientific

Anti-drug antibodies (ADAs) to therapeutic proteins could interfere with efficacy of treatment, and need to be monitored during clinical development. A case study will be presented where an automated and high performance specific ImmunoCAP ADA Bridging assay was used to detect ADAs to infliximab in a global multicenter study. Characterization of the assay demonstrates high sensitivity, drug tolerance and inter-laboratory precision, which enable robust transfer between laboratories and the use in multicenter studies.

1:45 Session Break

2:15 Chairperson’s Remarks
Jim McNally, Ph.D., Senior Principal Scientist, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

2:20 Development and Characterization of a Non-Cell-Based Assay to Assess the Presence of Neutralizing Antibodies to Interferon-Beta in Clinical Samples

Isabelle Cludts, Ph.D., Biotherapeutics, National Institute for Biological Standards and Control (MHRA, UK)

Different cell-based assay formats are available for detection of neutralizing anti-IFN-β antibodies. To overcome the limitations of these assays, a non-cell-based assay has been developed, utilizing an ECL detection platform. Neutralizing antibody titers in clinical samples from multiple sclerosis patients treated with IFN-β were determined and compared with those obtained using cell-based assays. The non-cell-based assay is less sensitive, however a good correlation between the two approaches was observed.

2:50 Immunogenicity Assessment Strategies and Assay Development for Enzyme Replacement Therapies

Stephen DeWall, Ph.D., Investigator, Clinical Immunology, GlaxoSmithKline

Enzyme replacement therapies (ERTs) have been successfully used to treat a number of rare, inherited diseases that are caused by deficiencies in specific metabolic enzymes. Although ERTs are typically highly immunogenic, they remain one of the most effective treatments for these disorders. Anti-ERT antibodies can potentially affect the safety and/or efficacy of these therapies, so monitoring patients for an immune response is vitally important. This presentation will cover immunogenicity testing strategies and assay development for ERTs.

3:20 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Re-Assessment of Immunogenicity Risk Based on Clinical Data: Case Study of a Humanized IgG1 Monoclonal Therapeutic with a Knob-and-Hole Structure

Mauricio Maia, Ph.D., Bioanalytical Sciences, Genentech, Inc.

Initial clinical immunogenicity evaluation plans are often based upon an immunogenicity risk assessment that includes a myriad of molecule and patient factors, but prior to attaining clinical experience. Clinical data can and should modify this assessment. This presentation will describe a case study of a structurally novel biotherapeutic whose risk-based assessment was changed following analysis of clinical immunogenicity data derived from early-stage trials.

4:30 Problem Solving Roundtable Discussions

Regulatory Expectations Regarding Immunogenicity Assessment
Laurie Graham, Ph.D., Product Quality Reviewer, Division of Monoclonal Antibodies FDA/CDER
Steven J. Swanson, Ph.D., Executive Director, Medical Sciences, Clinical Immunology, Amgen, Inc.

Drug Interference and Other Challenges with the Development of Neutralizing Antibody Assays

Renuka C. Pillutla, Ph.D., Director, Bioanalytical Sciences – Biologics, Bristol Myers Squibb

Dealing with Pre-Existing Positive ADA Activity in Study Patients
Moderator: Jim McNally, Ph.D., Senior Principal Scientist, Biotherapeutics Research, Pfizer, Inc.

Critical Issues in ADA Assay Validation
Moderator: Harry Yang, Ph.D., Senior Director, Translational Sciences, MedImmune, LLC

Concerns Regarding Immunogenicity of Multi-Domain Proteins
Moderator: Laura Salazar-Fontana, Ph.D., Former CDER/FDA

Focus on Immunogenicity of Biosimilars and Non-Innovator Biologicals
Moderator: Bridget Heelan, MB, Ph.D., Vice President, Consulting, Parexel, (ex-MHRA)

5:30 Welcome Reception in the Exhibit Hall with Poster Viewing

6:30 End of Day One of Immunogenicity Assessment & Clinical Relevance
TUESDAY, NOVEMBER 18

8:30 am Chairperson’s Remarks
Stephen DeWall, Ph.D., Investigator, Clinical Immunology, GlaxoSmithKline

REGULATORY PERSPECTIVES AND RISK ASSESSMENT

8:35 The Impact of Quality Attributes on Immunogenicity
Susan Kirshner, Ph.D., Associate Chief, Laboratory of Immunology, Therapeutic Proteins, Biotechnology, CDER/FDA

9:05 The Problems in Assessing and Comparing Immunogenicity of Biosimilars with the Reference Product
Bridget Heelan, M.B., Ph.D., Vice President, Consulting, Parexel, (ex-MHRA)
As biosimilars are not 100% identical to the originator this raises safety and regulatory concerns about relative immunogenicity. Comparing the results of ADA detection rates in the innovator and the biosimilar relies on an appropriate testing strategy. The advantages and limitations of comparing the results derived from a single assay or two separate assay formats will be presented.

KEYNOTE PRESENTATION

9:35 Strategy for Immunogenicity Risk Assessment
Steven J. Swanson, Ph.D., Executive Director, Medical Sciences, Clinical Immunology, Amgen, Inc.
Immunogenicity assessment continues to be an important component of the development of therapeutic proteins. Establishing an appropriate “risk-based approach” to testing for immunogenicity involves evaluating several factors including: whether the protein therapeutic will be used in a chronic or an acute dosing regimen; if there is an endogenous counterpart for the protein therapeutic, what the likely consequences of a neutralizing immune response would be, and what the predicted immunogenicity of the therapeutic would be. Understanding these factors will greatly assist in developing an appropriate strategy to follow in assessing immunogenicity during clinical trials.

10:05 Detection of Anti Drug Antibodies to a Therapeutic Using a Photonic Ring Immunoassay
Martin Gleeson, Ph.D., CSO, Genalyte, Inc
Recent data demonstrates the exceptional growth in biologic therapeutics across all phases of development. Often, patients taking infused or injected therapeutics can develop antibodies against the drug (ADAs). These ADAs can cause a decrease in efficacy, increased clearance rate, or adverse events. Genalyte has developed an assay capable of detecting and isotyping ADAs with sensitivity and drug tolerance levels exceeding regulatory guidelines. The assay demonstrated concordance with orthogonal technologies while yielding multiplex isotyping profiles, including IgG4.

CLINICAL INVESTIGATIONS

11:30 Statistical Considerations in Design of Multi-Tiered Methods to Detect and Confirm the Presence of ADAs in Clinical Studies
Harry Yang, Ph.D., Senior Director, Translational Sciences, MedImmune, LLC
Biopharmaceuticals have an inherent propensity to elicit immunogenic responses. Key to successful evaluation of immunogenicity is to have well developed and validated assays. This talk will focus on statistical strategies related to ADA assay validation, sample size determination, and cut point estimation in the presence of outliers and skewed distributions. In addition, we will explore ways to combine information from screening and confirmatory assays, so as to derive the optimal cut point.

12:00 pm Impact of Higher Order Complexes on Biomarker Target Quantitation
Surendran Rajendran, Ph.D., Senior Research Investigator II, Bioanalytical Sciences, Biologics, Bristol-Myers Squibb
During bioanalysis, quantitating the target, a biomarker, the drug interfered by an undesired higher order complex formation through multivalent interactions with target and assay reagents. This complex formation follows bell shaped concentration dependence with drug concentration which seems to explain the observed non-linear inverse relationship between immunogenicity and drug exposure. Its formation was confirmed in vitro by light scattering technologies.

12:30 End of Immunogenicity Assessment & Clinical Relevance

“Nice meeting; good mix of assays, technologies and experimental science.”
Anu C., Senior Scientist, Biomarin
TUESDAY, NOVEMBER 18

1:00 pm Conference Registration

2:00 Chairperson’s Opening Remarks
Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.

**SUB-VISIBLE PARTICLES, AGGREGATES, IMPURITIES AND IMMUNOGENICITY**

2:05 Innate Immune Response Modulating Impurities and Immunogenicity Risk: What Should We Be Looking for?
Daniela Verthelyi, Ph.D., Chief, Immunology Lab, Therapeutic Proteins, FDA/CDER
A critical factor associated with product immunogenicity is the presence of innate immune response modifying impurities (IIRMIs) that can stimulate the immune response directly. This talk will discuss the need to assess common impurities that activate immune cells in vivo and describe new in vitro systems that can be used to assess them.

2:35 Assessment of the Immunogenic Potential of Antibody Aggregates in Transgenic Mice
Juliana Bessa, Ph.D., Scientist, Immunopathology, F. Hoffmann-La Roche
Transgenic (tg) mice expressing a mini-repertoire of human IgG1 antibodies (Ab) have been used for the assessment of immunogenicity of therapeutic Abs. The tg mice were found to be tolerant to a large range of human IgG1 Abs. Immunization with IgG1 aggregates generated by three different stress conditions demonstrated that extensive modifications within the primary amino acid structure (neoepitopes) were required to break immune tolerance whereas mimerization may have an enhancer factor on the immune response triggered by the neoepitopes. Taken together, this IgG tg mouse model appears suited to identify potentially immunogenic modifications in Ab preparations.

3:05 Detection and Characterization of Reversible Self-Association and Aggregation of Therapeutic Monoclonal Antibodies
Sophia Levitskaya, Ph.D., Scientist, Analytical Biotechnology, MedImmune LLC
Protein self-association is a form of solution intermolecular interaction which is important to consider during the successful development of protein therapeutics. Protein reversible self-association behavior is difficult to evaluate because the conditions of an assay can influence the observed size distribution. Our case study describes an unusual temperature sensitive reversible self-association (RSA) of an IgG2-subclass mAb, analytical methods tailored to characterize RSA, and measures to minimize RSA in drug product.

3:35 Influence of Aggregates on in vitro T Cell Responses
Gary Bembridge, Ph.D., Director, Scientific Affairs, Immunology, Business Development, Antitope Limited

**ENHANCED IMMUNOLOGICAL PERFORMANCE WITH REDUCED IMMUNOGENICITY / IMMUNOGENICITY RISK PREDICTION**

4:30 Computational and Experimental Mapping of Deimmunized Biotherapeutic Design Space
Karen E. Griswold, Ph.D., Associate Professor, Thayer School of Engineering, Dartmouth
We describe novel protein design algorithms that simultaneously optimize biologics for reduced immunogenic potential and high-level molecular function. Using combinatorial optimization methods, we are able to rapidly design an entire suite of “Pareto optimal” variants whose predicted immunogenicities and activities are not simultaneously dominated by any other single design. We have redesigned two different therapeutic enzyme candidates, and here we discuss in vitro and in vivo demonstration of their enhanced molecular and immunological performance.

5:00 Prediction of Clinical Immunogenicity of Adnectins: Guiding Lead Optimization
Darren Forman, Ph.D., Principal Scientist, Immunogenicity Prediction, Bristol-Myers Squibb
Protein biologics are making up an ever increasing proportion of the total drug market. Unlike their chemical counterparts, proteins are large enough to induce an anti-drug antibody (ADA) response. Here, we will discuss our strategy to predict ADA generation, and a few examples for minimizing the immunogenic potential of therapeutic proteins in the discovery stage.

5:30 Panel Discussion: Development and Application of Humanized Mice for Immunogenicity Predictive Studies
Moderator: Jack Ragheb, Ph.D., Principal Investigator, Therapeutic Proteins, FDA/CDER
- How predictive are these models: To what extent does the HLA restriction of a single humanized mouse clone impact on the interpretation of the results?
- What information can these mice provide regarding B cell responses: the classes of antibody being produced and the levels of antibody?
- Time, investment and skill in getting mouse models up and running
- How to work out the appropriate dose
- Applications and recent progress with biotherapeutics: e.g. recombinant cytokines, gene therapy, etc.
- How might known differences in the human and mouse adaptive and innate immune systems impact the results?
6:00 End of Day One of Immunogenicity Prediction & Mitigation

6:00 Dinner Short Course Registration

6:30 – 9:30 Dinner Short Courses*
SC3: Immunogenicity Risk Assessment and Regulatory Strategy
SC4: Strategic Bioassay Design and Analysis

*Separate Registration Required. See page 3 for course details.

WEDNESDAY, NOVEMBER 19

PREDICTION AND SUPPRESSION

8:00 am Chairperson’s Remarks
Jack Ragheb, Ph.D., Principal Investigator, Therapeutic Proteins, FDA/CDER

8:05 Forecasting Clinical Immunogenicity from Human ex vivo/in vitro Assays
Tim Hickling, Ph.D., Associate Research Fellow, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

Although prediction of the incidence of anti-drug antibodies (ADAs) to therapeutic proteins is not yet possible, combining knowledge of the immunogenicity risk factors for a therapeutic protein enables assessment of overall risk. A mathematical model has been developed to integrate immunogenicity risk parameters and assay outputs to enable forecasting of ADA incidence and magnitude, and the impact of ADAs on PKPD. Examples of therapeutic proteins will be discussed.

8:35 Investigations in Immune Suppression for Monoclonal Antibody Therapeutics
Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.

Therapeutic proteins (TP) are often immunogenic and can induce formation of anti-drug antibodies (ADAs) when administered to preclinical animal models. The ADA formation may neutralize the pharmacologic activity of the TP and hence impact the exposure and efficacy by modulating its pharmacokinetics (PK) properties and clearance via immune complexes. The objective of this study is to assess the impact of immune suppression on the ADA formation and consequent impact on PK profiles of a biotherapeutic mAb. This talk will evaluate immune suppressive regimens targeting the T and B cells that can help reduce this unwanted immune response to a biotherapeutic mAb in a preclinical setting.

9:05 Preclinical Immunogenicity Risk Assessment for Optimal Lead Selection
Noel Smith, Ph.D., Senior Group Leader, Lonza Biologics, Lonza Applied Protein Services, Lonza

The ability to assess the “developability” of a therapeutic candidate in early preclinical and clinical phases of development can be a very powerful tool to enhance the chance of success. This presentation will focus on how immunogenicity risk assessment can be incorporated into a wider developability platform, exploiting a wide range of in silico and in vitro tools to predict immunogenic responses and the overall developability profile of lead candidates.

9:35 Problem Solving Roundtable Discussions

Risk Factors that Contribute to Immunogenicity
Moderator: Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.

Sub-Visible Particles, Aggregates and Immunogenicity
Moderator: Jack Ragheb, Ph.D., Principal Investigator, Therapeutic Proteins, FDA/CDER

Methods for Examining Impurities that May Impact the Immune Response
Moderators: Daniela Verthelyi, Ph.D., Chief, Laboratory of Immunology, Therapeutic Proteins, FDA/CDER
Lydia Haile, Ph.D., Postdoctoral Fellow, Laboratory of Immunology, Therapeutic Proteins, FDA/CDER

Current Tools and Approaches for Immunogenicity Risk Prediction
Moderator: Tim Hickling, Ph.D., Associate Research Fellow, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

Progress towards Inducing Immunological Tolerance to Factor VIII and Other Biotherapeutics
Moderator: David C. Wrath, Ph.D., Professor, Experimental Pathology, University of Bristol, & CSO, Apitope International NV

10:35 Coffee Break in the Exhibit Hall with Poster Viewing

IMPACT OF ROUTE OF ADMINISTRATION

11:15 The Effect of Route of Administration on the Immunogenicity to Recombinant Murine Growth Hormone Particles
Merry Christie, Scientist, Pharmaceutical Sciences, University of Colorado

Mice were injected with recombinant murine growth hormone (rmGH) via the subcutaneous, intraperitoneal, or intravenous (i.v.) routes. In addition to soluble, monomeric rmGH, the samples contained either nanoparticles of rmGH or both nano- and microparticles of rmGH. We found that multiple mechanisms contributed to the immune response, with the most pronounced response when i.v. administration was used. No dependence of the immune response on particle size and distribution was observed.

11:45 Reverse Vaccination via the S.C. Route to Mitigate Immunogenicity
Sathy Balu-Iyer, Ph.D., Professor, Pharmaceutical Sciences, SUNY-University at Buffalo

Administration of therapeutic proteins via the subcutaneous (s.c.) route is challenging regarding unwanted immune responses. This talk will focus on mechanistic details into factors driving immunogenicity of proteins given via the s.c. route. Based on this mechanistic insight, a novel Reverse Vaccination strategy to mitigate immunogenicity was applied. The talk will discuss the induction of immunological hypo-responsiveness using this strategy.
12:15 pm Tools and Technologies for Comprehensive Immunogenicity Risk Management
Emilee Knowlton, Sales Specialist, Immunology, ProImmune Inc.
Low immunogenicity is a key product attribute of successful biotherapeutics. This talk provides an overview of the technologies available for immunogenicity risk management including antigen presentation assays, DC-T cell assays to measure responses to formulated biologics, HLA-peptide Binding Assays, and naïve T cell Proliferation Assays to quantify responses to individual epitopes. The potential risk of a cytokine storm first infusion reaction can also be determined using whole-blood cytokine release assays.

12:45 Networking Lunch in the Exhibit Hall with Poster Viewing
(Sponsorship Opportunity Available)

TOLERANCE MECHANISMS

1:45 Chairperson’s Remarks
Tim Hickling, Ph.D., Associate Research Fellow, Pharmacokinetics, Dynamics and Metabolism, Pfizer, Inc.

KEYNOTE PRESENTATION
1:50 Immune Tolerance Induction for Therapeutic Proteins: The FDA Perspective
Amy Rosenberg, Ph.D., Director, Therapeutic Proteins, FDA/CDER
Immune responses to therapeutic proteins can prove devastating when they abrogate the efficacy of life saving therapeutic proteins or cause anaphylaxis. Immune tolerance induction (ITI) protocols have been developed to either prevent or reverse such destructive immune responses in the setting of enzyme replacement therapy (ERT) for Pompe Disease, a rare lysosomal storage disease (LSD). The safety of these regimens supports their use for ERT in the setting of other LSDs in patients predicted to respond to ERT with a robust antibody response, and, potentially, for patients where many doses can be given, but are less active in patients with solid tumors because their immune system makes anti-drug antibodies which inactive the immunotoxin. To suppress the immune response we have identified and largely silenced the T cell epitopes responsible for the immune response. A redesigned immunotoxin with T cell epitope mutations is highly cytotoxic to cell lines and to cells isolated from cancer patients and produces complete remissions in mice with human cancer xenografts. The approach described can be applied to de-immunize other therapeutically useful foreign proteins.

2:20 Generation of Antigen-Processing Independent Epitopes (APITOPES) for Induction of Tolerance to Factor VIII and Other Protein Antigens
David C. Wraith, Ph.D., Professor, Experimental Pathology, University of Bristol, & CSO, Apitope International NV
Suppression of immune responses to therapeutic proteins or hypersensitivity diseases currently requires the use of non-specific, immunosuppressive agents. Improved treatment can be achieved through the adoption of natural, immunoregulatory mechanisms. Scientists at Apitope have revealed how to design the peptide epitopes associated with these conditions and administer them in order to reinstate an immunological balance. This presentation will demonstrate that epitopes are a safe and improved approach to antigen-specific immunotherapy.

2:50 Networking Refreshment Break

3:15 Tolerogenic Nanoparticles for the Prevention of Anti-Drug Antibodies
Kei Kishimoto, Ph.D., CSO, Selecta Biosciences
Anti-drug antibodies (ADAs) can adversely affect the safety and efficacy of biologic drugs. We will describe the development of Synthetic Vaccine Particles (SVPs) for the induction of antigen-specific tolerance to prevent ADAs, using coagulation Factor VIII for the treatment of haemophilia A and adalimumab for the treatment of arthritis as examples.

3:45A Recombinant Immunotoxin for Cancer Treatment with Low Immunogenicity by Identification and Silencing of Human T Cell Epitopes
Ronit Mazor, Ph.D., Post Doctoral Fellow, Laboratory of Molecular Biology, National Cancer Institute, NIH
Recombinant immunotoxins have produced complete remissions in leukemia patients where many doses can be given, but are less active in patients with solid tumors because their immune system makes anti-drug antibodies which inactive the immunotoxin. To suppress the immune response we have identified and largely silenced the T cell epitopes responsible for the immune response. A redesigned immunotoxin with T cell epitope mutations is highly cytotoxic to cell lines and to cells isolated from cancer patients and produces complete remissions in mice with human cancer xenografts. The approach described can be applied to de-immunize other therapeutically useful foreign proteins.

4:15 Tregitope - A Natural Immune System Off-Switch for Antigen-Specific Tolerance Induction
Annie S. de Groot, Ph.D., Research Professor & Director, Immunology and Informatics, University of Rhode Island
Tregitopes are regulatory T cell (Treg) epitopes found in IgG that expand and activate natural Tregs and can be coupled to biologic proteins for antigen-specific tolerance induction. They are currently being integrated into products such as blood factors, enzyme replacement proteins and pharmaceutical toxins. The speaker will present recent Tregitope research validating antigen-specific tolerance induction and discuss their role in the treatment of immune-mediated diseases and the development of better biologics.

4:45 End of Immunogenicity Prediction & Mitigation

“I was a pleasure being at the conference: very high quality!”
Melody S., Senior Expert, Immunogenicity and Bioanalysis, TNO, a Netherlands Applied Research Center
TUESDAY, NOVEMBER 18

1:00 pm Conference Registration

2:00 Chairperson’s Opening Remarks
David Lansky, Ph.D., President, Statistics, Precision Bioassay, Inc.

SELECTING THE RIGHT BIOASSAY

2:05 Development of MOA Reflective Cell-Based Potency Assays for Biologic Products Involved in T Cell Co-Signaling Pathways
Shihua Lin, Ph.D., Analytical Biotechnology Development, MedImmune LLC

Potency assays play a key role at all stages of product lifecycle from early development to finished products. Due to increasing diversity and complexity of product formats as well as clinical targets, developing and optimizing MOA (mechanism of action) reflective cell-based potency assay could be challenging. This presentation will highlight general considerations and our approaches used to develop validatable cell-based potency assays for biologic products involving T-cell co-signaling pathways.

2:35 Selecting the Best Bioassay Format to Assess mAb Stability
Natko Nuber, Ph.D., Biologics R&D, Novartis

An ideal bioassay should mimic the MoA and be able to detect changes in the integrity of the drug. A case study of two related mAbs, specific for the same epitope of a membrane target, is presented. Temperature stressed and post-translationally modified samples were tested in four different bioassays; the different bioassays generated divergent results, suggesting that caution is needed when selecting the most appropriate bioassay format for membrane-bound targets.

3:05 Improving Heparin Bioassays by Following USP <1032>
David Lansky, Ph.D., President, Statistics, Precision Bioassay, Inc.

The recently revised USP monograph on the Heparin bioassay includes specific recommendations, several options for replication strategies, and offers users the choice of slope ratio or parallel line analyses. The recommended design imposes a split-unit design (USP <1032>). Recognizing that the assay design is a split-unit leads to useful insights about ways to improve the assay design and analysis. The split-unit design used has very low power for similarity testing in a parallel line analysis, but good power for similarity testing in a slope ratio analysis. Hence, for the Heparin bioassay (and related assays), the slope ratio analysis is a poor choice. The impact of these choices will be illustrated with data.

3:35 Non-Wash Immunoaassays and Label-Free Assay Platforms for Development of Immunogenicity Assays for Known Biosimilars
Lindsay Nelson, Ph.D., Application Scientist, PerkinElmer

We will show how Alpha Technology and label-free technology can be used as an alternative to ELISA or electro-chemiluminescence in immunogenicity and anti-drug-antibody assays. We will combine the use of antibodies to known biosimilars with PerkinElmer’s assay technologies to demonstrate several ways to improve your current methods for measuring immunogenicity.

3:50 Refreshment Break in the Exhibit Hall with Poster Viewing

STRATEGIES FOR MOLECULES WITH MULTIPLE MECHANISMS

4:30 Bioassays for Antibody Maytansinoid Conjugates (AMCs) Having Multiple Activities
Gillian Payne, Senior Director, Bioanalytical Science, ImmunoGen, Inc.

All AMCs have potent maytansinoid-directed anti-tumor activity. Some AMCs also have additional antibody-directed anti-tumor activity. A control strategy for such AMCs will be presented.

5:00 Development of a Simultaneous Binding Assay to Determine Potency of a Bispecific Zbody
Palanisamy Kanakaraj, Ph.D., Associate Director, Pharmacology, ZymoGen, Inc.

Zybodies are multi-specific antibodies generated by fusion of specific peptides to scaffold antibodies. We have developed a simultaneous binding assay to determine potency of a bi-specific zbody. The ability of the assay to measure the changes in potency of bi-specific zbody against each target molecule was determined. Comparability studies with ligand binding and cell based functional assays will be discussed.

5:30 KEYNOTE PRESENTATION
Characterization of Response of Multiple Domain Biotherapeutics
Jaya Goyal, Ph.D., Director, Translational Sciences, Biogen Idec

Many biotherapeutics currently in development have complex mechanisms of action and contain more than one domain, each with a specific role or function. As it is beneficial to align industry standards for evaluating immunogenicity of MDBs, this presentation highlights pertinent immunogenicity risk factors and describes steps involved in the design of a testing strategy to detect and characterize binding (non-neutralizing and neutralizing, NAb) ADAs.

6:00 End of Day One of Optimizing Bioassays for Biologics

6:00 Dinner Short Course Registration

6:30 – 9:30 Dinner Short Courses*
SC3: Immunogenicity Risk Assessment and Regulatory Strategy
SC4: Strategic Bioassay Design and Analysis

* Separate Registration Required. See page 3 for course details.
Wednesday, November 19

Comparability and Characterization Case Studies

8:00 am Chairperson's Remarks
8:05 Presentation to be Announced
8:35 Comparability Studies for Bioassays: Technical and Regulatory Challenges for Commercial Products
Jan Bohuslav, Ph.D., Scientist, Global Biologics Quality Control, Method Management and Technology (MMTech), Genentech, Inc., A Member of the Roche Group
For commercial products, both technical and regulatory requirements need to be considered when replacing or updating the licensed potency methods. A well-designed comparability assessment with meaningful acceptance criteria, which is dependent on the capability of the method, and should be evaluated case by case, is key to technical success and regulatory acceptance.

9:05 Case Study: Product Characterization, Sponsored by PK and Immunogenicity Assays for the Development of Biosimilar Trastuzumab
John Kamerud, Ph.D., Scientific Director, Eurofins Pharma Bioanalytical Services
In assessing the comparability of proposed biosimilar compounds to the innovator counterparts, regulatory agencies have stressed the "totality-of-evidence" approach, which relies on both structural and functional characterization, as well as data from animal and clinical studies. We present as a case study a package of assay methods developed for one such biosimilar, trastuzumab, which will include characterization of target binding, Fc receptor binding and ADCC activity as well as PK and immunogenicity assays to be used in clinical studies. Challenges encountered and approaches taken in the development of these methodologies will be discussed.

9:35 Problem Solving Roundtable Discussions

Strategies for Bioassays with Multiple Mechanisms
Moderator: Gillian Payne, Senior Director, Bioanalytical Science, ImmunoGen, Inc.

Selecting the Right Bioassay
Moderator: Natko Nuber, Ph.D., Biologics R&D, Novartis

Maintaining Assay Consistency
Moderator: LaKenya Williams, Ph.D., Senior Research Investigator I, Bioanalytical Sciences - Biologics, Bristol-Myers Squibb

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

Maintaining Assay Consistency

11:15 Preventing False Data Reporting: A Cell-Based Neutralizing Antibody Assay Case Study
LaKenya Williams, Ph.D., Senior Research Investigator I, Bioanalytical Sciences - Biologics, Bristol-Myers Squibb
Cell-based neutralizing antibody assays are inherently variable. Inadequate assay controls, including baseline samples and performance monitoring, can make cell-based assays particularly vulnerable to false data reporting. The FDA recognizes the difficulty in determining the degree of inhibition that is accurately indicative of neutralizing antibodies in a clinical sample. The recommendation is that the determination should be statistically based and derived using naive patient samples. This presentation will discuss various statistical approaches utilized for establishing Nab assay cut point and how we have managed inter-patient variability to ensure high data integrity during clinical trials.

11:45 Evaluation of Assay Consistency Over the Life Cycle of a Product
Janet Lathey, Ph.D., Consultant, Product and Assay Development and Evaluation
During product development and evaluation, critical assays undergo modifications. Assay results from preliminary studies often need to be bridged to those of pivotal studies. A testing and statistical approach to evaluate the consistency of assay results before and after assay modifications will be presented.

12:15 pm Sponsored Presentations (Opportunities Available)

12:45 Networking Lunch in the Exhibit Hall with Poster Viewing (Sponsorship Opportunity Available)

New Assay Technologies and Formats

1:45 Chairperson’s Remarks
Janet Lathey, Ph.D., Consultant, Product and Assay Development and Evaluation

1:50 Bioassay Automation in the QC Setting
Julie TerWhee, Ph.D., Quality Control, Analytical Sciences, Amgen, Inc.

2:20 High-Throughput Antibody Selection and Screening Methods for Improved Downstream Developability
William Roach, Ph.D., Scientist, Antibody Engineering and Platform Transfer Manager, Adimab, LLC
Antibody developability issues, such as aggregation and low solubility, can be reduced by employing specificity reagents during antibody discovery. These discovery approaches as well as high throughput methods for tracking antibody self or cross-interaction will be discussed.

2:50 Networking Refreshment Break
REGULATORY EXPECTATIONS

3:15 KEYNOTE PRESENTATION

The Science and Regulation of Potency Assays for Assessing the Quality of Biopharmaceuticals
Baolin Zhang, Ph.D., Senior Investigator, Therapeutic Proteins, Biotechnology Products, FDA

Assay adequacy is assessed by taking account of multiple factors including, but not limited to, product type, history, mechanism(s) of action (MoA), associated risk, phases of development, and quality data from physicochemical and biochemical testing. This presentation provides an overview of regulatory expectations regarding potency assays and discusses several case studies that highlight some of the relevant issues commonly seen in the regulatory submissions.

3:45 Compendial Potency Assays and Associated Biological Reference Materials – Challenges in Assay Transition and Unit Maintenance
Maura C. Kibbey, Ph.D., Senior Scientific Liaison, Biologics & Biotechnology, U.S. Pharmacopeia

With increasing frequency, especially for legacy biologics, animal assays are being replaced by in vitro assays of different formats. This transition is not always straightforward, as analysts may struggle to establish equivalence between assays that measure different attributes or sets of attributes. This presentation will focus on USP's current efforts to include modern in vitro assays in the USP-NF to replace animal-based tests for well-characterized biologics.

4:15 End of Optimizing Bioassays for Biologics

Conference Venue and Hotel

Hyatt Regency Bethesda
One Bethesda Metro Center
Bethesda, MD 20814
Tel: 301-657-1234
www.bethesda.hyatt.com

Discounted Room Rate: $189 s/d
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Mon - Tue am, November 17-18
C1 Immunogenicity Assessment & Clinical Relevance
C2 Immunogenicity Prediction & Mitigation
C3 Optimizing Bioassays for Biologics

Tue pm - Wed, November 18-19

SHORT COURSES

One short course
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Pre-Conference Short Courses
Sunday, November 16
1:30-4:30 pm SC1 Basics of Immunogenicity Testing
5:30-8:30 pm (Dinner Course) SC2 Challenges of Immunogenicity Assessment

Dinner Short Courses
Tuesday, November 18, 6:30-9:30 pm
SC3 Immunogenicity Risk Assessment & Regulatory Strategy
SC4 Strategic Bioassay Design and Analysis

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