CHI's Fifth Annual

Immunogenicity Summit 2013

November 11-13, 2013
Hyatt Regency on Capitol Hill
Washington, DC

TECHNOLOGIES AND STRATEGIES FOR SAFE AND EFFICACIOUS PRODUCTS IN THE CLINIC

KEYNOTE SPEAKERS:

Ranjana Advani, M.D., *Saul A. Rosenberg Professor of Lymphoma, Professor of Medicine/Oncology,* **Stanford Cancer Institute**

Kathleen Clouse, Ph.D., *Director, Division of Monoclonal Antibodies,* **CDER/FDA**

Ira Pastan, M.D., *NIH Distinguished Investigator, Co-Chief, Laboratory of Molecular Biology, National Cancer Institute,* **National Institutes of Health**

Max L. Tejada, Ph.D., *Senior Scientist, Biological Technologies,* **Genentech, Inc.**

Join 300+ of Your Peers!

CONCURRENT CONFERENCES

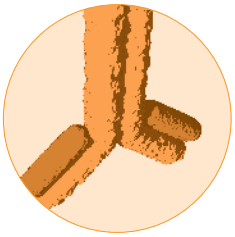
NOVEMBER 11-12

Immunogenicity Assessment & Strategies

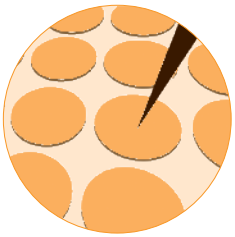
PK/PD of Novel Constructs

NOVEMBER 12-13

Immunogenicity Risk Assessment & Mitigation



Optimizing Bioassays for Biologics



PLUS! 5 Short Courses

ORGANIZED BY
Cambridge Healthtech Institute

ImmunogenicitySummit.com

About the Summit

Get ready to join 300+ of your peers from November 11-13, 2013 in Washington, DC at the #1 Immunogenicity Summit in the U.S.

CHI has an established reputation as a global education provider on immunogenicity. Our 2013 summit will build on last year's successful event. With double the number of tracks this year, the Immunogenicity Summit 2013 presents technologies for safety and efficacy from bench to bedside. For early stage decision-making on drug design and optimization, we examine the causes of immunogenicity together with means of mitigation, and present PK/PD and bioassay strategies. For later preclinical and clinical stages, we examine the complexities of immunogenicity assays, bioassays and PK/PD development, and present risk assessment strategies for smooth interaction with the regulatory authorities and safe and efficacious products in the clinic.

Sponsorship, Exhibit, and Lead Generation Opportunities

CHI offers comprehensive sponsorship packages which include presentation opportunities, exhibit space and branding, as well as the use of the pre and post-show delegate lists. Customizable sponsorship packages allow you to achieve your objectives before, during, and long after the event. Signing on early will allow you to maximize exposure to qualified decision-makers!

Agenda Presentations

Showcase your solutions to a guaranteed, highly-targeted audience. Package includes a 15 or 30-minute podium presentation within the scientific agenda, exhibit space, on-site branding and access to cooperative marketing efforts by CHI.

Breakfast & Luncheon 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. 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 high-level conference delegates. Speak face-to-face with prospective clients and showcase your latest product, service, or solution.

Inquire about additional branding opportunities!

Looking for additional ways to drive leads to your sales team? CHI can help through:

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- Experienced marketing team promotes campaign, increasing awareness and leads

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CHI also offers market surveys, podcasts, and more!

To customize your participation at this event, please contact:

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CONFERENCE SHORT COURSES*

SUNDAY, NOVEMBER 10

1:30 - 4:30 pm SC1: Basics of Immunogenicity Testing for Innovators and Biosimilars

Instructors:

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

Melody Sauerborn, Senior Expert, Immunogenicity and Bioanalysis, TNO, a Netherlands Applied Research Center

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 cutpoints
- Preclinical and clinical considerations
- Common problems

5:30 - 8:30 pm Dinner SC2: Challenges of Immunogenicity Assessment for Innovators and Biosimilars

Instructors:

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

Melody Sauerborn, Senior Expert, Immunogenicity and Bioanalysis, TNO, a Netherlands Applied Research Center

This interactive session of intermediate 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
- Regulatory guidance and guidelines

5:30 - 8:30 pm Dinner SC3: PK/PD Bioanalysis for Novel Biotherapeutics

Sponsored by GYROS

Moderator: Robert Durham, Ph.D., Director, Field Applications Scientists, GYROS, Inc.

Lee Abberley, Ph.D., Team Leader, DMPK, GlaxoSmithKline, US

Lindsay E. King, Ph.D., Senior Principal Scientist, Pfizer Inc

Novel constructs, such as anti-drug conjugates (ADCs) and bispecific antibodies, now exist as promising candidates in biotherapeutic pipelines. With aggressive timelines and contraction in the biopharma labor force, assay development can pose challenges beyond typical assays for pharmacokinetics and pharmacodynamics. Several bioanalytical techniques can be employed to measure these novel constructs. This short course will cover assay technologies to measure ADCs and bispecific antibody therapeutics for pharmacokinetics and pharmacodynamics presented by various biopharma scientists.

TUESDAY, NOVEMBER 12

6:15 - 9:00 pm Dinner SC4: Immunogenicity Risk Assessment and Regulatory Strategy

Instructors:

Laurie Graham, Product Quality Reviewer, Division of Monoclonal Antibodies FDA/CDER

Susan Kirshner, Ph.D., Associate Chief, Laboratory of Immunology, Therapeutic Proteins, Biotechnology, CDER/FDA

Robin Thorpe, Ph.D., FRCPath, Head, Biotherapeutics Group, National Institute for Biological Standards and Control

Christopher J. Holloway, Ph.D., Dr.rer.hum.biol.habil., Group Director, Regulatory Affairs & Chief Scientific Officer, ERA Consulting Group

The following topics will be covered:

- Priorities for the regulator: Hierarchy of concerns; data requirements; common gaps
- Integrated approach: Risk identification; aligning identified risks with CMC, bioanalytical, nonclinical and clinical strategy; ongoing risk management
- 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

Topics to be discussed include:

- 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 - 9:00 pm Dinner SC5: Developing Potency Assays to Ensure Successful Biologics

Instructor: Nancy Sajjadi, M.Sc., Independent Quality Consultant

This interactive short course will enable attendees to develop methods and strategies for developing and validating bioassays that support the identification and development of their biotherapeutics products. It will include coverage of assays to test both activity and potency, including cell-based and biochemical based systems.

** Separate Registration Required*

5TH ANNUAL | NOVEMBER 11-12

Immunogenicity Assessment & Strategies

Managing the Complexities for Innovators and Biosimilars

MONDAY, NOVEMBER 11

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.

Overcoming Challenges of Immunogenicity Assays

8:35 Novel Platform Using LC-MS and Ligand Binding Assays for Characterizing PK and Immunogenicity of ADCs
Melody Sauerborn, Senior Expert, Immunogenicity and Bioanalysis, TNO, a Netherlands Applied Research Center
Bioanalysis of antibody-drug conjugates is challenging. This is partially due to the heterogeneous mixture of different antibody-drug ratio (DAR) species and the different characteristics of the drug (small molecule), linker and antibody (large molecule). This talk will give a small introduction into ADCs, how size of molecule influences characterization technique, demonstrate how different companies have used different approaches to measure ADCs and introduce a novel platform for ADC characterization and measurement.

9:05 Case Study on Assessment of Neutralizing and Cross-Reacting Antibodies
Jim McNally, Ph.D., Senior Principal Scientist, Biotherapeutics Research, Pfizer, Inc.
Neutralizing antibody assays present a challenge for many bioanalytical laboratories. The choice of assay format (competitive ligand binding vs. cell based assay, for example), the identification of a positive control, and the timing of their implementation all are critical steps in the bioanalytical support for clinical immunogenicity assessment. This talk will focus on case studies addressing these challenges, the choices we made and the lessons we learned from each assay.

9:35 Immunogenicity Assessment Challenges for Nanobody® Programs: Strategies and Case Studies to Overcome Drug and Target Interference
Lieselot Bontinck, M.Sc., Scientist, Pharmacology, Bioanalytics & Immunogenicity, Ablynx N.V.

Sponsored by Genalyte

10:05 Multiplex Assays for Simultaneous Detection and Isotyping of Anti-Drug Antibodies Using Silicon Photonic Biosensors
Martin Gleeson, Ph.D., CSO, Genalyte, Inc.
Genalyte has developed a silicon chip based detection system, MaverickTM, which simultaneously measures multiple analytes from small samples in real time. The system eliminates virtually all sample preparation and has broad application in biotherapeutic research. In this presentation we will describe the principal of operation and show data generated using our multi-tier ADA assay for the simultaneous detection and isotyping of ADAs in a rapid and easy to use workflow.

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

11:15 Identification and Mitigation of Matrix Interference in Cell-Based Nab Assays
Martin Schwickart, Ph.D., Scientist, Clinical Pharmacology and DMPK, MedImmune, Inc.
To support biologics development in the clinic, neutralizing antibody assays are currently mandated by the FDA. The development of cell-based assays has significant challenges, especially regarding sensitivity and specificity. We present here a case where initially matrix interference was prohibitively high. We demonstrate a hypothesis-driven approach on how the source of matrix interference was identified, and eliminated with minimal sample manipulation.

11:45 Integrated Immunogenicity Data Analysis: Clinical Trial Results from a Biotherapeutic for the Treatment of Age-Related Macular Degeneration
Kyra J. Cowan, Ph.D., Scientist, BioAnalytical Sciences, Genentech, Inc.
Ranibizumab (Lucentis®) is a humanized anti-VEGF F(ab) approved by the FDA for the treatment of vision loss due to wet AMD, macular edema following retinal vein occlusion, and diabetic macular edema. The HARBOR study was designed to evaluate its safety and efficacy with intravitreal injection for the treatment of wet AMD over a two-year period. This talk will describe the approaches taken for the analysis of anti-therapeutic antibodies (ATAs) in sera from 1097 patients, and how the data interpretation informed the impact of ATAs on clinical endpoints.

Sponsored by Lonza

12:15 pm Preclinical Immunogenicity Risk Assessment Incorporated into a Developability Platform for Optimal Lead Selection
Noel Smith, Ph.D., Lead Scientist, Lonza Biologics
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 that includes *in silico* and *in vitro* tools to predict immunogenic responses as well as the potential manufacturability issues (aggregation, post translational modifications) that themselves have the potential to impact immunogenicity.

12:45 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

Immunogenicity Road Map/Change Implementation

2:15 Chairperson's Remarks
Kyra J. Cowan, Ph.D. Scientist, BioAnalytical Sciences, Genentech, Inc.

2:20 Developing a Strategy for Immunogenicity Assessment
Francesca Civoli, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.

2:50 TV-5010 and Efforts to Modify COPAXONE®: A Case Study on the Immunogenicity Impact on Safety and Regulatory Considerations for Complex Drugs
Jill B. Conner, Ph.D., Director, Global Specialty Medicines, Teva Pharmaceuticals
COPAXONE® is approved for the treatment of relapsing-remitting multiple sclerosis. COPAXONE® is a highly complex heterogeneous mixture of synthetic proteins / polypeptides with immunomodulatory activity. Teva had pursued development of a higher molecular weight version of COPAXONE® (TV-5010) by introducing changes to the COPAXONE® downstream synthesis procedure. The treatment with TV-5010 in animals led to severe side effects. This case study will examine both products and the differences in their immunogenicity profiles.

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

Concerns about Immune Complexes

4:00 A Case Study: Immune Complexes without Anti-Drug Antibodies. What Does it Mean?
Deborah Finco, Ph.D., Senior Principal Scientist, Drug Safety R&D, Pfizer, Inc.
Immune complexes may form in animals/people who receive protein biotherapeutic drugs, as a result of the development of anti-drug antibodies or due to other factors. Immune complexes can pose safety issues if they are not adequately cleared from the body. Often vasculitis or glomerular deposition are hallmarks of excessive amounts of immune complexes or deficiencies in the ability to remove them from circulation. This talk will highlight a nonclinical case study involving immune complexes with a biotherapeutic drug that did not induce anti-drug antibodies.

4:30 Problem Solving Roundtable Discussions

Table 1: Regulatory Expectations Regarding Immunogenicity Assessment
Moderator: Kathleen Clouse, Ph.D., Director, Division of Monoclonal Antibodies, FDA/CDER

Table 2: Challenges in Developing Neutralizing Antibody Assays
Moderator: Jim McNally, Ph.D., Senior Principal Scientist, Biotherapeutics research, Pfizer, Inc.

Table 3: Dealing with Pre-existing Positive ADA Activity in Study Patients
Moderator: Steven J. Swanson, Ph.D., Executive Director, Medical Sciences (Clinical Immunology), Amgen, Inc.

Table 4: Practical Application of Immunogenicity Preclinical Risk Assessment
Moderator: Kyra J. Cowan, Ph.D. Scientist, BioAnalytical Sciences, Genentech, Inc.

Table 5: Detection of Immune Complexes and Their Impact on Immunogenicity Assessment
Moderator: Deborah Finco, Ph.D., Senior Principal Scientist, Drug Safety R&D, Pfizer, Inc.

Table 6: Immunogenicity Testing During Clinical Trials
Moderator: Martin Schwickart, Ph.D., Scientist, Clinical Pharmacology and DMPK, MedImmune, Inc.

Table 7: Concerns Regarding Immunogenicity of PEGylated Proteins
Moderator: Laura Salazar-Fontana, Ph.D., Senior Staff Fellow and Immunogenicity Program Coordinator, Therapeutic Proteins, CDER/FDA

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

6:30 End of Day One of Immunogenicity Assessment & Strategies

TUESDAY, NOVEMBER 12

8:30 am Chairperson's Remarks

Jim McNally, Ph.D., Senior Principal Scientist, Biotherapeutics research, Pfizer, Inc.

Focus on Specific Products: ADCs and PEGylated Proteins

8:35 Immunogenicity Assessment for Antibody-Drug Conjugates

Marta Starcevic Manning, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.

Biotherapeutics containing multiple domains, such as antibody-drug conjugates (ADCs), require careful assessment of the immunogenicity monitoring strategy. ADC administration may result in antibody responses against the monoclonal antibody and/or linker/cytotoxin portions of the molecule. Immunogenicity assays should be able to detect antibodies against all components. Epitope characterization may be useful in ascertaining whether different types of responses have unique impact. Risk assessment, method development challenges and preliminary nonclinical and clinical immunogenicity results will be presented.

9:05 Regulatory Expectations and Experiences Regarding Immunogenicity of PEGylated Proteins

Laura Salazar-Fontana, Ph.D., Senior Staff Fellow and Immunogenicity Program Coordinator, Therapeutic Proteins, CDER/FDA

Pegylation of therapeutic proteins is believed to reduce their immunogenic potential. Published clinical data shows that antibodies directed against the PEG moiety pre-exist in the normal population and can be further induced upon exposure to pegylated therapeutics. Furthermore, the detection of these antibodies correlates, in certain instances, with increased drug clearance and adverse reactions. The impact of anti-PEG antibodies in the efficacy and safety of currently approved pegylated therapeutics will be presented to facilitate the understanding of current regulatory recommendations.

9:35 Potential Immunological Response to a PEGylated Protein Therapeutic after Chronic Administration

Anu Cherukuri, Ph.D., Senior Scientist, Pharmacological Sciences, BioMarin, Inc.

Pegylation was first introduced as a way to extend the half-life of protein therapeutics and reduce immune-mediated clearance. Despite this original intention, there have been several reports of anti-PEG antibody development associated with decreased therapeutic half-life and increased hypersensitivity reactions. The immunologic mechanism of the anti-PEG antibody response will be reviewed in this presentation. Understanding and anticipating the anti-PEG antibody response may help guide the clinical dosing regimen of some PEGylated proteins and increase the likelihood of these drugs moving forward in the clinical development process.

10:05 Innovative Uses of Acid Treatment to Improve Immunogenicity Testing and LBA for Pharmacokinetic Assessment

Sponsored by Tandem Labs LabCorp Clinical Trials

Manju Saxena, Ph.D., Group Leader, Principal Scientist, Tandem Labs, a LabCorp Company

Complementary methods with acid treatment will be discussed to mitigate 1) interference by anti-drug antibodies (ADA) on ligand-binding pharmacokinetic (PK) assays, and 2) masking of ADA activity in immunogenicity assays due to high concentrations of biologic drug. These methods are applicable to the bioanalysis of peptide drugs and anti-drug antibodies.

10:20 Poster Presentation

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

Pre-Existing Antibodies

11:10 Impact of Pre-Existing Antibodies on the Safety and Clinical Pharmacology of a Novel Anti-TNF Alpha Receptor 1 Therapeutic.

Claire Holland, Ph.D., Senior Manager, Biopharm R&D, Clinical Immunology, GlaxoSmithKline

Pre-existing antibodies are frequently encountered during immunogenicity assessments. However, their relevance in terms of the safe and effective administration of a therapeutic protein is still poorly understood. Here we present a case study where pre-existing antibodies altered the safety and clinical pharmacology of a novel TNF alpha receptor 1 therapeutic in a preliminary clinical trial involving healthy subjects. We will discuss the *in vitro* and clinical investigations that were conducted and the risk factors that contributed to the clinical outcome.

US and EU Regulatory Concerns

11:40 EU Perspectives on Assessing Unwanted Immunogenicity of Non-Innovator Products and Biosimilars

Robin Thorpe, Ph.D., FRCPath, Head, Biotherapeutics Group, National Institute for Biological Standards and Control

Unwanted immunogenicity of biological medicines continues to be a serious problem and can have serious clinical consequences. It is a concern for regulators assessing biological products and the EU CHMP was the first regulatory agency to publish a guideline on the subject in 2008. Determining the immunogenicity of biosimilar products requires similar assessment approaches to stand-alone products, but in addition comparative immunogenicity studies with the reference product are required. Issues relating to the above will be considered including immunogenicity concerns with non-innovator products.

» KEYNOTE PRESENTATION

12:10 FDA Perspectives on Issues Regarding Immunogenicity for Monoclonal Antibodies

Kathleen Clouse, Ph.D., Director, Division of Monoclonal Antibodies, FDA/CDER

This talk will address challenges with pre-existing antibody; how excess drug interferes with the assays; novel issues that are not anticipated by clinicians; the potential of emerging antibody products for greater immunogenicity; attempts to increase half-life that may render products more immunogenic; overcoming Immunogenicity to TNF antagonists; and the importance of post-licensing monitoring.

12:40 End of Immunogenicity Assessment & Strategies

2ND ANNUAL | NOVEMBER 11-12

PK/PD of Novel Constructs

Optimizing Bispecific Antibodies and ADCs

MONDAY, NOVEMBER 11

7:30 am Registration and Morning Coffee

8:40 Chairperson's Opening Remarks
Nahor Haddish-Berhane, Ph.D., Senior Principal Scientist, Pfizer

Clinical Experience with PK/PD of Novel Constructs

» KEYNOTE PRESENTATION:

8:50 Impact of Brentuximab Vedotin in the Treatment of Lymphoma
Ranjana Advani, M.D., Saul A. Rosenberg Professor of Lymphoma, Professor of Medicine/Oncology, Stanford Cancer Institute
The recent FDA approval of Brentuximab vedotin (ADCETRIS®) an anti CD 30 antibody drug conjugate represents a major therapeutic advance in Hodgkin Lymphoma and Anaplastic Large Cell Lymphoma therapy after almost three decades. Pivotal trials report overall response rates exceeding 70% in patients with relapsed or refractory disease. These results, have led to investigation of Brentuximab vedotin in the front line setting in combination with chemotherapy and is rapidly changing the standard of care of CD30-positive lymphoproliferative malignancies.

9:35 Trends in Novel Constructs: Quality Attributes That May Impact PK or Mechanism of Action
Marjorie A. Shapiro, Ph.D., Chief, Laboratory of Molecular and Developmental Immunology, Division of Monoclonal Antibodies, FDA/CDER
Current trends in antibody development include novel constructs, cocktails, antibody-drug conjugates and Fc engineering to enhance or reduce effector function or to enhance PK. This presentation will highlight current trends in MAb development with a focus on analytical studies and control strategies to support the development of novel products.

10:05 Sponsored Presentation *(Opportunity Available)*

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

Nonclinical PK/PD of ADCs: Where Are the Opportunities for Improvement?

11:15 PK-PD Considerations in the Development of Antibody-Maytansinoid Conjugates
Jan Pinkas, Ph.D., Director, Pharmacology, ImmunoGen, Inc.

11:45 Exploiting the Properties of Fleximer™ to Improve Pharmacokinetics: Applications to Small Molecules, Biologicals, and Antibody-Drug Conjugates
Timothy B. Lowinger, Ph.D., CSO, Mersana Therapeutics
Fleximer is a highly biocompatible, fully biodegradable polyvalent polymer with unique properties, which include tremendous water solubility, plasma stability, and the ability to improve pharmacokinetics and biodistribution. Examples of the application of Fleximer to improve the drug-like qualities of proteins, small molecules and antibody-drug conjugates will be presented.

12:15 pm Sponsored Presentation *(Opportunity Available)*

12:45 Luncheon Presentations *(Sponsorship Opportunities Available)* **or Lunch on Your Own**

Use of Mechanistic PK/PD Modeling

2:15 Chairperson's Remarks
Nahor Haddish-Berhane, Ph.D., Senior Principal Scientist, Pfizer

2:20 Does It Take Two or Four to Tango? Modeling & Simulation of Bispecific Antibodies in Oncology
Tamara Van Steeg, Ph.D., Senior Consultant PK/PD, LAP&P Consultants BV
Modeling and simulation is a powerful tool to aid understanding in complex systems with multiple interactions. As such, M&S is especially useful in the development of bispecific antibodies by assessing the interactions of these molecules with its biological target already at an early stage. The interplay of M&S activities, experimental data and available knowledge on the system (e.g. receptor densities) will provide guidance on the strategies for further development of these drugs.

2:50 Could We Have a Ballpark Idea about Tumor Targeting Prior to the Accurate Measurement?
Guozheng Liu, Ph.D., Research Assistant Professor, Radiology, University of Massachusetts Medical Center
This talk introduces a very simple kinetic model that considers a solid tumor as a "reactor," aiming to prepare researchers to get some information about tumor accumulation with less efforts or prior to feasible measurement. It will rationalize the authors' observations on tumor accumulation by pretargeting, summarize them into "rules of thumb", and provide some general insights to tumor accumulations.

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

4:00 Guiding ADC Development by Employing PK/PD Modeling and Simulation Approaches
Nahor Haddish-Berhane, Ph.D., Senior Principal Scientist, Pfizer
The talk will highlight a diverse set of multi-scale models, including a PBPK model for ADC, which can used to support ADC programs at various development stages. Two different case studies will be presented to demonstrate the utility of PK/PD models for preclinical-to-clinical translation of ADC efficacy. Use of mathematical models to guide the discovery of ADC and precision medicine approach will be briefly discussed.

4:30 PK/PD Modeling to Determine Individual Dose Response
Rakesh Sindhi, M.D., Professor of Surgery, Co-Director, Pediatric Transplantation, Children's Hospital of Pittsburgh
Anticipating efficacy and safety before early or late phase clinical trials can promote informed use of novel drugs and regimens. PK/PD modeling of immunosuppressant(s) using *ex-vivo* cell-based assays will be discussed to illustrate several uses for clinical drug development. These uses include identifying effective doses and biomarkers which can be used as companion diagnostics and surrogate endpoints.

» 5:00 pm PANEL DISCUSSION WITH SPEAKERS

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

6:30 End of Day One of PK/PD of Novel Constructs

TUESDAY, NOVEMBER 12

Nonclinical PK/PD of Multi-Specific Modalities

8:30 am Chairperson's Remarks

Benno Rattel, Ph.D., Executive Director, Nonclinical Development ARM, AMGEN Research (Munich) GmbH

8:35 Discovery Phase Support for Large Molecule Therapeutics with Multiple Specificities: New Challenges in Bioanalytical and Pharmacokinetic Assessment

Chris Macaraeg, Senior Associate Scientist, PKDM, Amgen

The future of large molecule therapeutics includes increasingly complex biologics with multiple target specificities. While there is an urgency to shorten discovery time, the complexity of these molecules creates additional bioanalytical challenges. Multiple ligand binding assays are necessary to fully assess their pharmacokinetic properties, determine their functional activities and identify potential biotransformation. The presentation will focus on the bioanalytical challenges associated with these multi-specific molecules and present case studies where different approaches were used to overcome these challenges.

9:05 PK Optimization of Bispecific DART Proteins for Clinical Use

Syd Johnson, Ph.D., Vice President, Antibody Engineering, MacroGenics, Inc.

Manufacturability, stability and pharmacokinetics have been challenges to effective development of bispecific antibodies for clinical use. We have developed and optimized several formats of our highly stable Dual-Affinity Retargeting (DART®) proteins that address these issues. Multiple examples will be presented of DART proteins approaching the clinic for oncology, autoimmunity or infectious disease applications. Challenges of nonclinical toxicology for these highly potent molecules in relevant species will also be discussed.

9:35 Testing Strategies for the Assessment of Bispecific T cell-engaging BiTE® Antibodies and Their Transition into the Clinic

Benno Rattel, Ph.D., Executive Director, Nonclinical Development ARM, AMGEN Research (Munich) GmbH

Bispecific T-cell engagers, commonly referred to as BiTE® antibodies, are comprised of two different flexibly linked single-chain antibodies, one directed against a tumor antigen and one targeting CD3. BITE® antibodies can transiently link tumor cells with resting polyclonal T-cells for induction of a surface target antigen-dependent re-directed lysis of tumor cells, closely mimicking a natural cytotoxic T-cell response. Strategies for nonclinical assessment and for defining a safe clinical starting dose, and lessons learnt in the clinic will be presented.

10:05 Sponsored Presentation *(Opportunity Available)*

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

pH-Dependent Binding Antibodies

11:10 Engineering of pH-Dependent Binding Antibodies for Improved Pharmacokinetics

Changshou Gao, Ph.D., Fellow, Antibody Discovery & Antibody Engineering, MedImmune

Antibody-mediated serum half-life extension of soluble antigens (antibody buffering) and receptor antigen-mediated antibody clearance can negatively impact antibody efficacy and increase the need for high dosing. Antibodies with pH-dependent binding can address both of these issues by offering decreased antibody buffering allowing better clearance of soluble antigens and reducing target-mediated clearance of receptor binding antibodies. We'll discuss different approaches to engineer pH-dependent mAbs for enhanced potency through improved pharmacokinetics.

11:40 PK Modeling of Sweeping Antibody; Antigen Sweeping Effect of Antibody with pH-Dependent Antigen Binding and Increased FcR Binding

Yuki Iwayanagi, Ph.D., Research Scientist, Preclinical Research, Chugai Pharmaceutical Co. Ltd.

Sweeping antibody with enhanced FcR-mediated cellular uptake of the antigen-antibody complex and pH-dependent endosomal antigen dissociation enables elimination of the antigen from plasma. Sweeping antibody provides novel approach to target antigens which was difficult to be targeted by conventional antibody. Using PK model analysis, we describe the antigen sweeping effect of sweeping antibody in comparison to conventional high affinity antibody.

12:10 pm End of PK/PD of Novel Constructs

HOTEL & TRAVEL

Conference Hotel:

Hyatt Regency Washington on Capitol Hill
400 New Jersey Avenue NW
Washington, DC 20001
Phone: 888-421-1442

Discounted Room Rate: $285 s/d
Discounted Room Rate Cut-off Date: October 14, 2013

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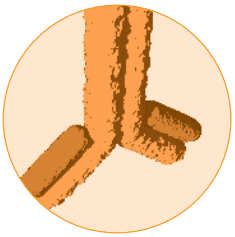


Immunogenicity Risk Assessment & Mitigation

Safe and Efficacious Products from Drug Discovery to the Clinic and Beyond

TUESDAY, NOVEMBER 12

2:00 pm Chairperson's Opening Remarks
Jack Ragheb, Ph.D., Principal Investigator, Therapeutic Proteins, FDA/CDER

Identification of Risk Factors

2:05 Understanding and Controlling Anti-Drug Antibody Responses to Enzyme Replacement Therapy; a Proposed Mechanism for Immune Tolerance Induction
Alexandra Joseph, Ph.D., Associate Scientific Director, Investigative Clinical Immunology, Clinical Laboratory Sciences Department, DSAR, Sanofi

2:35 Evaluation of Immunogenicity Risk of Biotherapeutics Targeting Dendritic Cell Receptors
Li Xue, Ph.D., Principal Scientist, PDM Immunogenicity Sciences, Pfizer, Inc.
Reliable immunogenicity risk assessment and mitigation is built upon accurate evaluation of immunogenicity risk factors that are associated with biotherapeutics. Several methods for risk assessment were developed and/or applied to investigate the immunogenicity risk of targeting dendritic cell receptors. The risk contribution to our understanding of the underlying causes of immunogenicity will be discussed.

3:05 A Pharmacogenetic Approach to Immunogenicity: Implications for Overcoming Attrition Owing to Development of Anti-Drug Antibodies during Clinical Trials Using Factor VIIa as a Model
Zuben E. Sauna, Principal Investigator, Hematology, FD/CDER
An algorithm based on an individual patient's genotype and MHC-II repertoire can be used to assess patient-specific immunogenic responses to therapeutic-proteins. To demonstrate the utility of this approach we will evaluate the immunogenicity-risk of neo-epitopes generated in two bio-engineered Factor VIIa products. The development of these products was recently discontinued due to the development of ADAs. The implications of identifying at risk patients and drug development based on pharmacogenetics will be discussed.

Sponsored by PROIMMUNE www.proimmune.com

3:35 Tools and Technologies for Comprehensive Immunogenicity Risk Management
Briana Betz, Ph.D., Immunology Sales Specialist, ProImmune, Inc.
ProImmune has developed a comprehensive suite of *in vitro* assays that characterize DC, T cell, B cell and innate immune responses. Antigen presentation assays using mass spectrometry, dendritic cell - T cell assays and physical HLA-peptide binding assay can be combined to provide a broad picture of protein antigenicity. Data from these assays can help inform improved drug design and lead selection through a clearer understanding of the mechanisms that drive immune responses.

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

Aggregate-Induced Immunogenicity/ Benefits of Mouse Models

4:30 Investigation of Immunogenicity Induced by Aggregates Using Immune-Tolerant Mice
Vera Brinks, Ph.D., Postdoctoral Researcher, Utrecht University, Utrecht Institute for Pharmaceutical Sciences; Currently Visiting Scientist, Therapeutic Proteins, FDA
Aggregation is a major risk factor for immunogenicity of therapeutic proteins. Nonetheless, the mechanisms by which aggregates induce the formation of antidrug antibodies are unknown. Here, I will present several studies on the characterization of aggregate-driven immunogenicity, focusing on its initiation and subsequent immunological processes including timing of CD4+ T-cell help, formation of germinal centers, and effect of immune modulating drugs on antibody levels. These studies are performed in immune tolerant mice.

5:00 Humanized Mouse Models for Nonclinical Immunogenicity Assessment of Novel Protein Therapeutics
Birgit Reipert, Ph.D., Director, R&D Immunology, Baxter BioScience
Current activities focus on the design of protein therapeutics with molecular and/or chemical modifications to improve the pharmacokinetic properties of these proteins. However, any of these modifications bears the risk of creating neoepitopes that could stimulate T-cells and/or B-cells. We developed new animal models for assessing the immunogenicity of such modified proteins during preclinical development. First results as well as advantages and limitations of these new models will be discussed.

» 5:30 PANEL DISCUSSION:

Relevance of Animal Models for Predicting the Immunogenicity of Therapeutic Proteins
Moderated by: Jack Ragheb, Ph.D., Principal Investigator, Therapeutic Proteins, FDA/CDER

- Pros and cons of humanized mice and transgenic mice
- 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
- Are relative immune responses (e.g. aggregated vs. non-aggregated human protein in a mouse) a valid measure?
- 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 Risk Assessment and Mitigation

6:00 Registration for SC4

6:30 – 9:00 Dinner SC4: Immunogenicity Risk Assessment and Regulatory Strategy*
Instructors to include: Laurie Graham, Product Quality Reviewer, Division of Monoclonal Antibodies FDA/CDER
Robin Thorpe, Ph.D., FRCPath, Head, Biotherapeutics Group, National Institute for Biological Standards and Control

**Separate Registration Required*

WEDNESDAY, NOVEMBER 13

Risk Considerations for Biotherapeutics

8:30 am Chairperson's Remarks

Haiyan Jiang, Ph.D., Senior Director, Preclinical and Clinical Research (Hemophilia), Biogen Idec, Inc.

8:35 Understanding the Immune Response against Erythropoiesis Stimulating Agents that Can Lead to Pure Red Cell Aplasia

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

Antibody-mediated PRCA (amPRCA) is characterized by bone marrow devoid of red blood cell precursors and circulating antibodies capable of neutralizing erythropoietin. The anti-erythropoietin antibodies that are associated with cases of amPRCA have different characteristics than the antibodies observed in subjects that do not have PRCA. Those antibodies associated with PRCA tend to be of the IgG4 subclasss, have a higher circulating level, bind to the protein region of erythropoietin, and are more likely to have neutralizing capability than the antibodies from patients that do not have PRCA. This observation underscores the value in developing and validating assays to fully characterize clinically relevant anti-therapeutic protein antibodies.

9:05 Late-Onset Hypersensitivity to an SC Administered Peptide Drug: Lessons Learned

Harald Kropshofer, Ph.D., Senior Personalized Healthcare Leader, Pharmaceutical Development, F. Hoffmann-La Roche Ltd.

A clinical case study will be presented focusing on a peptide drug that gave rise to serious systemic hypersensitivity (SSH) in clinical phase 3. The case study will emphasize essentially three aspects which appear to be key for the understanding of drug-induced and anti-drug antibody-mediated hypersensitivity reactions: (i) the requirement of multiple risk factors that coincide, (ii) the diversity of underlying mechanisms leading to SSH, (iii) the fact that SSH may not be seen prior to clinical phase 3. Different ways of mitigating the risk of SSH will be discussed.

9:35 Novel Antibody Therapeutics with Engineered Features and Impact on Immunogenicity: Case Study of the Effect of an FcRn Mutation

Sally Fischer, Ph.D., Senior Scientist and Group Leader, Bioanalytical Research & Development, Genentech, Inc.

To improve the effectiveness of antibody therapeutics, a variety of antibodies with engineered features have been generated. These engineered features are designed to improve various characteristics of the molecules. This presentation will focus on a case study where a mutation intended to increase FcRn binding affinity caused unforeseen challenges in the immunogenicity evaluation of the molecule.

10:05 Designing Therapeutic Drugs with Reduced Immunogenicity

Gary Bembridge, Ph.D., Business Development Manager, Antitope (Polytherics Company)

The importance of T cell help has been widely accepted as a significant risk factor in the development of anti-drug antibodies (immunogenicity). Case study data will be presented on the deimmunisation of naturally immunogenic non-human protein therapeutics.

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

Measures to Reduce Immunogenicity

» KEYNOTE PRESENTATION

11:15 Novel Approach to B and T Epitope Removal from Immunotoxins with Retention of High Cytotoxic Activity

Ira Pastan, M.D., NIH Distinguished Investigator, Co-Chief, Laboratory of Molecular Biology, National Cancer Institute, National Institutes of Health

Recombinant Immunotoxins are chimeric proteins designed to kill cancer cells. They are composed of an Fv that binds to a cancer cell and a protein toxin that kills the cell. RITs have produced complete remissions in over 50% of patients with refractory Hairy Cell leukemia but in some patients antibodies form preventing complete remission. We have developed novel experimental approaches for the identification and removal of B and T cell epitopes. The properties of new immunotoxins predicted to have low immunogenicity in humans will be described.

11:45 Problem Solving Roundtable Discussions

Table 1: Product-Related Factors that Contribute to Immunogenicity

Moderator: Jack Ragheb, Ph.D., Principal Investigator, Therapeutic Proteins, FDA/CDER

Table 2: Identification and Silencing of Immunogenic Epitopes

Moderator: Ira Pastan, M.D., NIH Distinguished Investigator, Co-Chief, Laboratory of Molecular Biology, National Cancer Institute, National Institutes of Health

Table 3: Prediction Technologies for Immunogenicity

Moderator: Harald Kropshofer, Ph.D., Senior Personalized Healthcare Leader, Pharmaceutical Development, F. Hoffmann-La Roche Ltd.

Table 4: Risk Assessment and Risk Management

Moderator: Steven J. Swanson, Ph.D., Executive Director, Medical Sciences (Clinical Immunology), Amgen, Inc.

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

2:00 Chairperson's Remarks

Harald Kropshofer, Ph.D., Senior Personalized Healthcare Leader, Pharmaceutical Development, F. Hoffmann-La Roche Ltd.

2:05 Integrated Computational and Empirical Identification of Anti-Drug Antibody Epitopes Supports Clinical Risk Assessment and De-Immunization of Therapeutic Proteins

Larry Kauvar, Ph.D., Senior Vice President, CSO, Trellis Bioscience

Although most Anti-Drug Antibodies (ADAs) are innocuous, some low abundance or low frequency ADAs may pose a significant clinical risk which is difficult to evaluate at the serum level. Trellis' established technology platform for cloning rare B-cells enables deconvolution of serum into its component monoclonal ADAs. Our computational epitope prediction technology accelerates cloning ADAs against all epitopes on the protein. The technology further enables efficient immunological silencing of problematic epitopes.

Tolerance Mechanisms

2:35 Evidence for Immune Tolerance Induction in Hemophilia A Mice Treated with Factor VIII Fc Fusion Protein

Haiyan Jiang, Ph.D., Senior Director, Preclinical and Clinical Research (Hemophilia), Biogen Idec

Inhibitors to factor VIII (FVIII) are a significant impediment in treating hemophilia A (HemA). In contrast to rFVIII, therapeutic doses of recombinant FVIII Fc fusion protein (rFVIIIFc) were shown to induce immune tolerance to FVIII in HemA mice, partially via interactions with FcRn and FcgR. In a recently completed phase 3 study in severe hemophilia A patients, rFVIIIFc was well tolerated, and no inhibitors were detected. The immune tolerance potential of rFVIIIFc merits further investigation in previously untreated patients.

3:05 Refreshment Break

3:30 Progress towards Inducing Immunological Tolerance to Factor VIII

David W. Scott, Ph.D., Professor and Vice Chair, Research, Medicine, Uniformed Services, University of Health Sciences, Bethesda

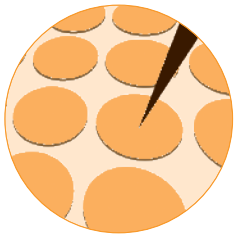
Many hemophilia A patients treated with therapeutic factor VIII (FVIII) produce neutralizing antibodies to the product, thus rendering this therapy ineffective. Recently, significant progress has been made to modulate this undesirable immune response. Methods to identify immunodominant epitopes in FVIII and the generation of T cell clones against FVIII have aided this progress. Novel approaches to induce tolerance using IgG fusion proteins, nanoparticles, gene therapy and specific T regulatory cells will be discussed.

4:00 Tolerogenic Nanoparticle-Based Immunotherapies to Inhibit Anti-Drug Antibody Responses

Takashi Kishimoto, Ph.D., Chief Science Officer, R&D, Selecta Biosciences

Anti-drug antibodies are a major concern for biological therapies and a particular challenge for biosimilars. Selecta Biosciences is a clinical stage company developing an entirely new class of tolerogenic nanoparticle-based immunotherapies to inhibit anti-drug antibody responses. We have demonstrated preclinical efficacy against model proteins and against human therapeutic proteins, such as Factor VIII and adalimumab. This presentation will provide insights into the application of tolerogenic nanoparticle immunotherapies in preclinical models that reduce immunogenicity and potentially improve the safety and efficacy profile.

4:30 Close of Immunogenicity Risk Assessment & Mitigation



Optimizing Bioassays for Biologics

Techniques and Solutions for Biotherapeutics Development

TUESDAY, NOVEMBER 12

2:00 pm Chairperson's Opening Remarks

Optimizing Bioassays: Challenges and Solutions

» KEYNOTE PRESENTATION

2:05 New Technologies and Approaches to Bioassays

Max L. Tejada, Ph.D., Senior Scientist, Biological Technologies, Genentech, Inc.

Cell-based potency assays can be the most challenging of analytical assays to develop. They are expected to reflect the mechanism of action (MOA) of the therapeutic but must also be suitable for use in a QC environment. Different antibody formats, an increasing diversity of clinical indications with complex MOAs, and reduced timelines due to increased competition, make assay development more challenging. Various approaches and strategies will be presented to address some of these challenges, including the incorporation of new technologies and formats, as well as the use of surrogate measures of bioactivity.

2:35 Optimization of Ligand Binding Assay by Design of Experiment

Surendran Rajendran, Ph.D., Senior Research Investigator, BAS - Biologics, Bristol-Myers Squibb

Biotherapeutics research uses predominantly Ligand Binding Assay to quantitate biomarker, biologic drug and its immunogenicity at preclinical and clinical stages to establish the PK/PD relationship and thus to accelerate drug development. Making ligand binding assay by Design of Experiment (DoE) methodology has many advantages over traditional one factor at a time method. An easy to do DoE protocol for ligand binding assay is described that optimizes the three main assay performance parameters sensitivity, dynamic range and the background simultaneously.

3:05 Development and Optimization of a Potency Assay for a 7 Component Peptide Drug

Barbara Hebeis, Ph.D., Principal Scientist, CMC Bioassay and Genomics, NDA Analytics

For drugs consisting of multiple active components, potency has to be demonstrated for all components individually.This talk focuses on the development of a bioassay for a multi peptide drug. The format selected for this example, based on the drug's mode of action, was the enumeration of drug activated T cells from primary murine splenocyte cultures isolated from animalsimmunised with individualpeptide components of the drug. Based on results demonstrating a moderate T cell response of ex vivo cultured and periodically re-stimulated rodent splenocytes we have developed a method suitable for routine, cGMP compliant potency testing using ELISpot for the detection of IL-2 released from activated T cells.

Reference Standards and Regulatory Expectations

3:35 Reference Standards for Potency Assays – Future Directions

Jane Robinson, Ph.D., Principal Scientist, Biotherapeutics, National Institute for Biological Standards and Control, UK

With increasing numbers of biopharmaceuticals in development, including next-generation (modified or artificial) molecules and biosimilars, meeting future requirements for publicly available reference standards for potency assays will be challenging. Parent molecules and innovator products may prove unsuitable as standards for corresponding next generation or biosimilar products, with relative potency determination proving either impossible or method-specific and resulting in a requirement for product-specific standards.

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

4:30 A Regulatory Perspective on Bioassays for Evaluation of the Quality of Protein Drug Products

Baolin Zhang, Ph.D., Senior Investigator, Division of Therapeutic Proteins, Office of Biotechnology Products, Food and Drug Administration

For all protein products, drug-specific potency assays are required to assess product quality because the complex protein structures cannot be inferred from physical-chemical characterizations alone. A suitable measure of potency is essential to assure the consistency of the product dose, the consistency of the manufacturing process, and the comparability of product lots. This talk presents the principles in the design of bioassays, regulatory perspectives, and case studies for bioassays used in the evaluation of protein products.

Assay Transition and Transfer

5:00 Compendial Potency Assays and Associated Biological Reference Materials – Challenges in Assay Transition and Unit Maintenance

Tina S. Morris, Ph.D., Vice President, Biologics & Biotechnology, United States Pharmacopeial Convention, Global Science & Standards Division

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.

5:30 A Statistical Approach to Bioassay Bridging and Transfer

Xianzhi Zhou, Ph.D., Senior Scientist, MedImmune

How does one bridge between bioassays? Assays frequently need to be replaced, whether it be a result of unsupported instrumentation or improved methodology. This talk will present a case study demonstrating how MedImmune approaches bioassay bridging and transfer using statistical guidance.

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

6:00 Registration for SC5

6:30 – 9:00 Dinner SC5: Developing Potency Assays to Ensure Successful Biologics *

Instructor: Timothy Schofield, Senior Fellow, MedImmune

**Separate Registration Required*

WEDNESDAY, NOVEMBER 13

Managing Variability

8:30 am Chairperson's Remarks

8:35 Regulatory-Compliant Validation of a Standardized ADCC Potency Assay

Alexis Rossignol, Ph.D., R&D Project Manager, Clean Cells SAS

Antibody-dependant cellular cytotoxicity (ADCC) is one of the major mechanisms of action of therapeutic monoclonal antibodies (mAbs), with a growing number of "ADCC-optimized" mAbs. Health Agencies require the use of biologically-relevant potency assays to characterize new mAbs and to release batches. But current ADCC assays are hampered by reproducibility and standardization issues, especially when they involve freshly isolated primary human cells (PBMC, NK…) as effector cells. In this context, Clean Cells and its partner INSERM UMR892 have developed an ADCC assay based on standardized CD16-expressing effector T cells. This presentation will show its outstanding performances in terms of accuracy, linearity, repeatability, reproducibility and sensitivity to mAb modifications (fucosylation…). These results were obtained in a validation study designed to meet EMA requirements and support the use of this robust assay for lot release.

9:05 Evaluation of Processes for Reducing and Monitoring Assay Variability for Bioassays

Janet L. Lathey, Ph.D., Director, Immunology and Assay Development, BioDefense Division, Emergent BioSolutions

Within the life cycle of a product several developmental phases of a bioassay usually occur. A major challenge with potency testing is the establishment of consistency of results by reducing and maintaining assay variability. Some essential processes to reduce and evaluate variability are 1) identification of assay components responsible for major assay variation; 2) identification and qualification of critical reagents; 3) bridging of reference sera to a "standard"; and 4) documented analyst training program.

Bioassay Automation Technology

9:35 Bioluminescent NFAT-RE-luciferase Reporter Bioassay: A Novel Technology to Reduce Assay Variability in ADCC

M.N. Dixit, Assistant General Manager & Head, Bioanalytical Laboratory, Clinigene International

Bioassays play a vital role in evaluating biological functions of protein biotherapeutics. Classic Antibody Dependent Cell Mediated Cytotoxicity (ADCC) assays involving Natural Killer cells are utilized for potency evaluation of therapeutic antibodies. However, high variability makes such assays less dependable for evaluating the targeted function of biologic drug products. The new bioluminescent NFAT-RE-luciferase reporter bioassay is ideal for evaluating Fc effector functionality of therapeutic antibodies in ADCC.

10:05 Sponsored Presentation *(Opportunity Available)*

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

11:15 Assay Development, Automation and De-Convolution of Multiplexed High Throughput Live-Cell Screens

Brad Greenfield, Scientist, Theraclone Sciences

Utilizing a live whole cell approach to Theraclones antibody screening platform, we are able to interrogate entire extra-cellular proteomes in a target-agnostic manner, and multiplex via pooled cell types to increase throughput and identify conserved epitopes/targets across multiple cell types. Assay design, automation, confirmation and de-convolution of multiplexed screening data will be presented.

11:45 From Spleen to Screen

Cecile Geuijen, Ph.D., Director, Oncology, Merus BV

Merus has developed and validated a powerful discovery engine for the discovery of potent and fully human bispecific antibodies targeting cancer: Biclonics™. Direct sequencing of antibody variableregions from the spleen of immunized MeMo® mice and subsequent co-expression of these antigen specific variable regions into bispecific moleculesusing automated multi-well systemsenables the rapid screening of thousands of unique Biclonics™ in *in vitro* functional assays. Lead candidates areidentified based on potent growth inhibition oftumor cells.

12:15 Problem Solving Roundtable Discussions

Table 1: Standardizing ADCC Potency Assays
Moderator: Alexis Rossignol, Ph.D., R&D Project Manager, Clean Cells SAS

Table 2: Meeting USP Standards for Bioassays
Moderator: Tina S. Morris, Ph.D., Vice President, Biologics & Biotechnology, United States Pharmacopeial Convention, Global Science & Standards Division

Table 3: Assay Automation to Decrease Variability
Moderator: Brad Greenfield, Scientist, Theraclone Sciences

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

Considerations for Biosimilars

2:00 Chairperson's Remarks

2:05 Special Considerations for Developing Cell-Based Immunogenicity Neutralizing Anti-Drug Antibody (NAb) Assays to Support Clinical Comparability Studies for Biosimilars

Xiao-Yan Cai, Ph.D., Director, Biologics Bioanalytical Development, Merck Research Laboratories

Immunogenicity assays are critical to support comparability studies to ensure safety and efficacy of a biosimilar in comparison with its originator biologic therapeutic drug per regulatory guidance. Demonstrating "equivalency" of the non-quantitative cell-based NAb assay to detect NAbs against both biosimilar and originator compounds presents unique challenges. Special considerations must be taken into account during assay development of these NAb assays.

2:35 Functional Assays for Biosimilars: An Industry Perspective

Patrick Liu, M.D., Ph.D., Senior Director and Global Head of Bioassays, Teva Pharmaceuticals, Inc.

Functional characterization of a biosimilar to its reference product is essential to biosimilar therapeutic development. With an appropriate assay strategy and clear understanding of regulatory expectations, development and implementation of validated biological assays can generate a successful regulatory submission package, and therefore, significantly contribute to the quality and success of the program, and as well as save the overall development time and cost.

3:05 Refreshment Break

Cell-Based vs. Non Cell-Based Assays

3:30 Comparison of Cell-Based and Non Cell-Based Assay Platforms for the Detection of Anti-Drug Neutralizing Antibodies

Jenny Hu, ATO Clinical Immunology, Medical Science, Amgen, Inc.

Different assay platforms have been used for the detection of neutralizing antibodies. Evaluations of these platforms were mostly focused on assay development and characterization; limited data were generated using clinical samples. In this study, non cell-based assays were developed and assessed for their ability to detect neutralizing antibodies as compared to its complementary cell-based assays. Case studies comprised of several therapeutic molecules and comparison of results from clinical samples will be discussed.

4:00 Non-Cell-Based Assay and Cell Based Assays In Support Of Antibody Development Programs

Jeffrey Barbon, Senior Scientist, Renal and Immunology Biologics (RIB), abbvie

Lead candidate antibody generation requires a battery of *in vitro* assays for characterization studies including functionality. Non-cell-based assays are typically an easy first step in the antibody screening process but the true quality of antibody leads must inevitably be established in cell-based functional assays. Several case studies will be highlighted.

4:30 Close of Optimizing Bioassays for Biologics

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Summit Pricing – Includes access to 4 conferences, excludes short courses.		
Registrations after October 11, 2013, and on-site	$2899	$1299
STANDARD CONFERENCE PRICING		
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Registration after October 11, 2013 and on-site	$1949	$979

Monday, November 11 - Tuesday, November 12	Tuesday, November 12 - Wednesday, November 13
(T1) Immunogenicity Assessment & Strategies	(T3) Immunogenicity Risk Assessment & Mitigation
(T2) PK/PD of Novel Constructs	(T4) Optimizing Bioassays for Biologics

SHORT COURSES		
One short course	$699	$399
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SC1: Basics of Immunogenicity Testing
Dinner SC2: Challenges of Immunogenicity Assessment
Dinner SC3: PK/PD Bioanalysis for Novel Biotherapeutics
Dinner SC4: Immunogenicity Risk Assessment and Regulatory Strategy
Dinner SC5: Developing Potency Assays to Ensure Successful Biologics

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