Third Annual

Immunogenicity Summit 2011

November 16-18

DoubleTree Hotel ■ Bethesda, Maryland

A 2-part event covering developments in assay technologies, risk assessment, regulatory guidance and means of predicting and avoiding immunogenicity

PART ONE:

Immunogenicity Assessment and Clinical Relevance

November 16-17

PART TWO:

Immunogenicity Prediction and Mitigation

November 17-18

Pre-Conference Short Courses

November 15

1: Technical Advice on Assay Development, Validation and Sample Analysis

2: Development of Neutralizing Antibody Assays

Course Instructors:

Deborah Finco, Ph.D., Immunogenicity Lead, Immunotoxicology COE, Drug Safety R&D, Pfizer, Inc.

Jaya Goyal, Ph.D., Principal Investigator, Clinical Science & Technology, Biogen Idec, Inc.

FEATURED PRESENTATIONS

Update on US Regulatory Guidance

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

European Update on Unwanted Immunogenicity of Biologicals and Biosimilars

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

Clinical Immunogenicity Testing Road Map: What We've Learned from Clinical Studies

Sue Richards, Ph.D., Group Vice President, Clinical Laboratory Sciences, Genzyme Corp.

Innate Immune Response Modulating Impurities

Daniela Verthelyi, M.D., Ph.D., Chief, Laboratory of Immunology, Therapeutic Proteins, CDER, FDA

Register by August 26th and SAVE up to $350!

Corporate Sponsors:

MSD Meso Scale Discovery

Phadia Now Thermo Fisher Scientific

Corporate Support Sponsor:

BioAgilytix Labs™ Ready Today to Enable Your Breakthroughs of Tomorrow™

ImmunogenicitySummit.com

ORGANIZED BY Cambridge Healthtech Institute

PRE-CONFERENCE SHORT COURSES*

Tuesday, November 15, 2011

SC1: TECHNICAL ADVICE ON ASSAY DEVELOPMENT, VALIDATION AND SAMPLE ANALYSIS

8:00 – 9:00 am Registration

9:00 – 12:30 pm Short Course

This interactive session will enable attendees to work out an immunogenicity pre-clinical and clinical testing protocol for their particular therapeutic protein. Recent advances will be presented and areas of difficulty will be addressed. Attendees are encouraged to contribute with their own experiences and to bring questions for discussion.

The following topics will be covered:

- Immunogenicity concerns for different types of product
- Assay methodologies
- Critical issues in assay validation
- Challenges to anticipate
- Application step to discuss sample analysis and any relevant issues

SC2: DEVELOPMENT OF NEUTRALIZING ANTIBODY ASSAYS

12:30 – 1:30 pm Registration

1:30 – 5:00 pm Short Course

Neutralizing antibodies not only affect efficacy of the therapeutic but also pose the danger of cross-reacting antibodies and ensuing adverse reactions. This interactive session is designed to enable attendees to work out how to design, develop and validate their assays for neutralizing antibodies, and to interpret the results. Attendees are encouraged to contribute with their own experiences and to bring questions for discussion.

The following topics will be covered:

- Strategy for design, development and validation
- Challenges to anticipate
- Interpretation of results
- Emerging trends
- Clinical implementation
- Regulatory guidance and guidelines

Instructors for both courses:

Deborah Finco, Ph.D., Immunogenicity Lead, Immunotoxicology COE, Drug Safety R&D, Pfizer, Inc.
Jaya Goyal, Ph.D., Principal Investigator, Clinical Science & Technology, Biogen Idec, Inc.

**Separate Registration Required*

Sponsorship & Exhibit Opportunities

Sponsors and Exhibitors will enjoy facilitated networking opportunities with 200 international scientists and executives. Enhance business development and lead generation initiatives by presenting and exhibiting your expertise to this targeted audience.

Sponsorship Opportunities

Agenda Presentations
Agenda presentation sponsorships include a 15 or 30-minute podium presentation within the scientific agenda of your choice, as well as exhibit space, onsite branding and access to the conference delegate lists.

Breakfast & Luncheon Presentations
These presentations include a 20 to 30-minute podium presentation with a 10 to 15-minute Q&A session. Invite session attendees to enjoy breakfast or lunch on your company's behalf while you give your talk.

Invitation-Only VIP/ Hospitality Suite
Sponsor will select invitees from the conference pre-registration list for an evening of networking at the hotel or a top local venue. CHI will extend invitations, conduct follow-up and monitor responses. Reminder cards will be placed in the badges of those delegates who will be attending.

Pre-Conference Workshops
Includes 15-minute or 30-minute podium presentation during pre conference workshop, as well as your company logo displayed on pre conference workshop materials and onsite signage.

Other Networking and Promotional Opportunities

- Branded Badge Lanyards
- Chair Drops
- Branded Tote Bags
- Tote Bag Insert
- Exhibit Hall Reception
- Refreshment Break
- Program & Exhibit Guide Sponsor

Exhibitor Information – SIGN UP BY AUGUST 1ST & SAVE $300!
Exhibitors will enjoy facilitated networking opportunities with 200 high-level decision-makers. Speak face-to-face with prospective clients and showcase your latest product, service or solution.

Sponsorship packages can be customized to meet your company's budget and goals.

For more information on sponsorship and exhibit opportunities, please contact:

Katelin Fitzgerald
Manager, Business Development, Cambridge Healthtech Institute
Ph: 781-972-5458, kfitzgerald@healthtech.com

Hotel & Travel Information

Conference Venue:
DoubleTree Hotel and Executive Meeting Center
8120 Wisconsin Ave
Bethesda, MD 20814
Ph: 301-652-2000

Discounted Room Rate: $229 s/d
Discounted Cut-off Date: October 19, 2011

Please visit our conference website to make your reservations online or call the hotel directly to reserve your sleeping accommodations. Identify yourself as a Cambridge Healthtech Institute conference attendee to receive the reduced room rate. **Reservations made after the cut-off date or after the group room block has been filled (whichever comes first) will be accepted on a space- and rate-availability basis. Rooms are limited, so please book early.**

For details on flight and car rental discounts, visit ImmunogenicitySummit.com

PART ONE:

IMMUNOGENICITY ASSESSMENT AND CLINICAL RELEVANCE

WEDNESDAY, NOVEMBER 16

7:30 am Registration and Morning Coffee

8:30 Chairperson's Opening Remarks
Stephen Keller, Ph.D., Associate Director, Pre-Clinical and Clinical Development Sciences, Abbott Biotherapeutics Corp.

ASSAY DEVELOPMENTS

8:35 Improved Methods for More Accurate Detection of Neutralizing Antibodies
Michael Tovey, Ph.D., Director, Research, Laboratory of Biotechnology & Applied Pharmacology, ENS Cachan
Conventional cell-based assays are sensitive to serum-matrix effects, have low drug tolerance, and are unsuitable for detection of NADAs against therapeutic monoclonal antibodies dosed at high concentrations and with prolonged washout rates. Case studies in RA and Crohn's disease show that both circulating levels of functional infliximab, adalimumab, and etanercept and NADAs can be quantified rapidly with the elimination of serum matrix effects using a standardized validated assay based on an engineered cell line.

9:05 Perspectives on Ligand Binding Assays for Immunogenicity Assessment
Marie T. Rock, Ph.D., Vice President, Protein Bioanalysis, Midwest BioResearch LLC, a Wil Research Company
This presentation will provide a perspective on using ligand binding assays for immunogenicity assessment and includes approaches and insights of the AAPS Ligand Binding Assay Focus Group Steering Committee. In addition, the difficulties and challenges encountered (reagents, patient population, controls, cut-point) will be discussed with approaches for successfully overcoming those difficulties and challenges using case studies.

9:35 A High-throughput Approach to Overcome High Levels of Drug Endogenous Counterpart in ADA Screening Assays
Sam Song, M.D., Senior Scientist, Immunoassay Development, Merrimack Pharmaceuticals, Inc.
When a drug is a counterpart of a major endogenous protein, often present in extremely high levels in the blood circulation, it is almost impossible to detect ADAs, even with acid dissociation because the ADA re-associates with the endogenous protein during the neutralization step after acid dissociation. This presentation will introduce a novel approach to detect ADAs in the presence of extremely high level of endogenous protein counterpart of drug.

10:05 How to Benefit from a Diagnostic Partner in the Assay Development
Sponsored by Phadia, Now Thermo Fisher Scientific
Speaker to be Announced, Pharmaceutical and Healthcare Collaborations, Thermo Fisher Scientific
With more than 40 years of expertise in the area of immunoassay development meeting clinical demands, Thermo Fisher Scientific can be a perfect match in your assay development. The expertise, experience and assay platforms are now accessible for you to develop R&D assays and/or clinical tests. Working with Thermo Fisher Scientific reduces assay development times and ensure high performance and if/when needed, world-wide supply.

10:20 Networking Coffee Break in the Exhibit Hall with Poster Viewing

11:00 The Pros and Cons of Acid Dissociation
Albert Torri, Ph.D., Senior Director, Bioanalytical Sciences, Regeneron Pharmaceuticals, Inc.
The drug tolerance of an immunogenicity assay determines the ability of the assay to detect ADA responses in the presence of drug in the sample. If drug levels in study samples are expected to be relatively high, incorporating an acid dissociation step into the assay may improve the detection of ADA. The use and issues associated with acid dissociation will be discussed.

11:30 Translation of Pre-Clinical Cytokine Assessments to Cytokine Release and Cytokine Release Syndrome in Humans Following MAb Treatment
Tobias Manigold, M.D., Lab Head, Immunosafety, Hoffmann-La Roche
Among IRRs, cytokine release syndrome (CRS) can cause major harm to patients and innovative drugs if encountered unexpectedly and without appropriate mitigation strategies. This presentation will provide insight to the value of pre-clinical *in vivo* and *in vitro* cytokine testing for the translation of CR(S) in humans. Moreover, the need for further validation of *in vitro* prediction systems to allow individualized prediction of CRS within the clinic will be discussed.

12:00 Impact of Assay Method Selection on ATA Data
Melissa Cheu, M.S., Principal Research Associate, BioAnalytical Assays, Genentech, Inc.
Immunogenicity data can be impacted by the methodology and format of the assay used to detect anti-therapeutic antibodies (ATAs). The use of different methodologies (ELISA, RIP, ECLA) for detection of ATAs to the same molecule can affect ATA data due to differences in relative sensitivity and drug tolerance between methods. Case studies of several assays will be presented.

12:30 Lunch on Your Own

1:55 Chairperson's Remarks
Michael Tovey, Ph.D., Director, Research, Laboratory of Biotechnology & Applied Pharmacology, ENS Cachan

» FEATURED PRESENTATION

2:00 Mice with a Human Immune System: Applicability and Use for Immunogenicity Studies
Kristina Howard, D.V.M., Ph.D., FDA Commissioner's Fellow, Therapeutic Proteins, Pharmaceutical Sciences, CDER, FDA
Humanized mouse models now permit assessment of antigen specific adaptive immune responses made in the context of human HLA. A variety of models will be reviewed including the benefits and limitations inherent with each model. Discussion will focus on the use of humanized mice in immunogenicity testing and drug development for a range of pharmaceutical products including biologics, drugs and devices.

PK/PD CASE STUDIES

2:30 Efficient Immunogenicity: Can We Streamline Non-Clinical Immunogenicity Assessment?
Holly W. Smith, B.A., Senior Research Scientist, Investigative Toxicology, Eli Lilly and Company
Recent white paper and guidance documents are triggering thought-provoking process change considerations. After years of discussing approaches to measure, confirm, and characterize anti-drug antibodies, is it possible that we may not need to perform these activities in most non-clinical studies? Is a weight of evidence approach a sufficient assessment? Is it appropriate to lengthen a study specifically for drug wash-out for ADA measurements? Case studies will be presented to discuss these questions, the issues that arise, and the impact on drug development from a non-clinical perspective.

3:00 Clinically Relevant Immunogenicity Testing from R&D to Clinic
Sponsored by Phadia — Now Thermo Fisher Scientific
Jörgen Dahlström, Ph.D., M.B.A., Senior Manager Marketing & Scientific Support, Phadia, now Thermo Fisher Scientific
Immunogenicity assessment of a biopharmaceutical drug's immunogenic potential is a challenging task. It involves developing a range of assays specific for the biological -a long, tedious and labour intense process, as these tests must be designed for transfer to CROs and eventually made available for companion diagnostics. Phadia, now thermo Fisher Scientific, has more than 40 years of expertise in the area of immunoassay development that meets clinical demands. We now offer access to both expertise and platforms, for you to develop R&D assays and/or clinical tests.

3:30 Networking Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Results from a Toxicokinetic Study of a Novel Protein
Matthias Hofmann, Ph.D., Senior Investigator I, TS-PCS-Biologics Safety and Disposition, Novartis Institutes for Biomedical Research
A novel protein was tested in a TK-study. Validation of assays developed to analyze PK, immunogenicity, and bioactive PK will be presented, as well as an integrated picture of the study results. Although anti-drug antibodies seem to target the Ag-binding site of the drug, neutralizing effects were not detected.

RELATIONSHIP BETWEEN HYPERSENSITIVITY AND IMMUNOGENICITY

4:30 Drug-induced Immune Complex-Mediated Hypersensitivity Reactions in the Non-Human Primate (NHP)
Daniel T. Mytych, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.

5:00 Report from Clinical and Laboratory Standards Institute on Design and Validation of Immunoassays for Assessment of Human Allergenicity of New Biotherapeutic Drugs
Robert G. Hamilton, Ph.D., D. ABMLI, Professor, Medicine and Pathology, Clinical Immunology and Allergy, Johns Hopkins University School of Medicine; Director, John Hopkins Dermatology, Allergy & Clinical Immunology Reference Laboratory
The CLSI I/LA34-P document provides a framework for the design and validation of a qualitative immunoassay that detects human IgE antibody to new drugs in various body fluids and tissue extracts. Unique challenges are discussed involving validation of a drug-specific IgE antibody assay in the absence of a positive IgE antibody control serum, minimization of interference by microgram/ml levels of IgG antibody in the detection of nanogram/ml levels of IgE antibody, and the potential for high non-specific binding when human test specimens are analyzed undiluted.

5:30 BREAKOUT SESSIONS

Table 1: Challenges in Developing Neutralizing Antibody Assays
Moderator: Michael Tovey, Ph.D., Director, Research, Laboratory of Biotechnology & Applied Pharmacology, ENS Cachan

Table 2: Benefits and Risks of the Competitive Ligand Biding Assays for Neutralizing Antibodies
Moderator: Marie T. Rock, Ph.D., Vice President, Immunoassays, Midwest BioResearch, a Wil Research Company

Table 3: Dealing with Pre-Existing Positive ADA Activity in Study Patients
Moderator: Stephen Keller, Ph.D., Associate Director, Pre-Clinical and Clinical Development Sciences, Abbott Biotherapeutics Corp.

Table 4: Practical Application of Immunogenicity Pre-Clinical Risk Assessment
Moderator: Holly W. Smith, B.A., Senior Research Scientist, Investigative Toxicology, Eli Lilly and Company

Table 5: Immunogenicity Testing During Clinical Trials
Moderator: Meena Subramanyam, Ph.D., Vice President, Translational Sciences & Technology, Biogen Idec, Inc.

Table 6: CLSI ILA-34 Guideline on IgE Anti-drug Assay Development and Validation
Moderator: Robert G. Hamilton, Ph.D., D. ABMLI, Professor, Medicine and Pathology, Clinical Immunology and Allergy, Johns Hopkins University School of Medicine, and Director, John Hopkins Dermatology, Allergy & Clinical Immunology Reference Laboratory

Table 7: What Does the FDA Expect From an Immunogenicity Program?
Moderator: Susan Kirshner, Ph.D., Associate Chief, Laboratory of Immunology, Office of Biotechnology, FDA

6:30 Networking Reception in the Exhibit Hall with Poster Viewing

7:30 End of Day One of Immunogenicity Assessment and Clinical Relevance

THURSDAY, NOVEMBER 17

7:30 – 8:15 am Breakfast Presentation

(Sponsorship opportunity available, please contact Katelin Fitzgerald, kfitzgerald@healthtech.com) **and Morning Coffee**

IMMUNOGENICITY IN THE CLINIC AND RELATION TO PRE-CLINICAL PREDICTIVE STUDIES

8:30 Chairperson's Remarks
Meena Subramanyam, Ph.D., Vice President, Translational Sciences & Technology, Biogen Idec, Inc.

8:35 Case Study on Immunogenicity Testing from Non-Clinical to Clinical
Deborah Finco, Ph.D., Senior Principal Scientist, Drug Safety R&D, Pfizer, Inc.
Xiaflex is a drug product comprised of two collagenase enzymes intended for the treatment of Dupuytren. Due to the localized administration of the drug, there is little/no systemic drug exposure. This presents some unique aspects to the program. This talk will concentrate on immunogenicity results and assays as well as some other endpoints used in the non-clinical and clinical studies. Post marketing commitments will also be presented.

» KEYNOTE PRESENTATION

9:05 Clinical Immunogenicity Testing Road Map: What We've Learned from Clinical Studies

Sue Richards, Ph.D., Group Vice President, Clinical Laboratory Sciences, Genzyme Corp.
The ability of a drug to elicit an immune response is routinely evaluated as a component of clinical development for biotherapeutics. However, immunogenicity assessment often does not end with just testing drug-specific antibodies and neutralizing antibodies. Additional characterization is often necessary in the context of safety or efficacy evaluations. A number of factors can be considered when implementing further in-depth analyses. Case examples will be presented to demonstrate approaches taken to support clinical programs and lessons learned.

9:35 Interference Observed During Immunogenicity Assessment of an Fc-Engineered Therapeutic Antibody
Sally Fischer, Ph.D., Senior Scientist & Group Leader, Bioanalytical Research and Development (BARD), Genentech, Inc.
An anti-therapeutic antibody response in patients depends on a number of factors including patient population, disease state, route of delivery or characteristics specific to the product. This presentation will discuss a case study where the challenges encountered during development of a clinical ATA assay were due to the specific patient population as well as the engineered therapeutic antibody.

10:05 A Streptavidin Coated Plate for Long-Term Clinical Studies

Sponsored by MSD Meso Scale Discovery

Pankaj Oberoi, Ph.D., Director, Scientific Services and Research & Development, Meso Scale Discovery
There is increasing demand for a streptavidin coated plate that satisfies the demands of long-term clinical trials, especially for immunogenicity studies. MSD® has made substantial investments in optimizing the production and characterization of reagents and manufacturing processes associated with the production of Streptavidin coated plates. The plates are subject to seven independent measurements of plate uniformity in a well-defined QC process. Furthermore, the plates maintain performance through a shelf life of 30 months, reducing the frequency of new lot validations. Data supporting the performance of the plates has been collected from over 4000 plates comprising 200 production lots over a two year period.

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

11:10 Detecting, Characterizing, and Dealing with Pre-Existing ADA in Clinical Studies
Stephen Keller, Ph.D., Associate Director, Pre-Clinical and Clinical Development Sciences, Abbott Biotherapeutics Corp.
ADA methods are becoming increasingly effective at identifying subjects that develop post-treatment antibody responses to biotherapeutics. Occasionally, however, very high assay signals are seen in samples from drug-naïve populations, raising the questions of what's being detected and what to do about it? This presentation will use case studies to illustrate this phenomenon and offer some perspective on what should be done to follow up such observations.

11:40 Cut Point Rules for Development of an ELISA to Detect Antibodies to a Clinically Asymptomatic Virus Infection
Brian Schlain, Lead, Non-Clinical Statistician, Biostatistics, Biogen Idec, Inc.
PML is a rare brain disease caused by the JC virus (JCV). A 2-step assay (ELISA screening + supplemental confirmation) was developed to detect anti-JCV antibodies in serum or plasma. While the false negative rate in the assay was determined using sera samples from urinary JCV DNA shedders who were assumed sero-positive for JCV antibodies, false positive rates could not be directly controlled, as JCV infection is asymptomatic.

12:10 pm Lunch on Your Own

COMBINED PLENARY SESSION: (PARTS ONE AND TWO)

12:30 pm Registration for Part Two

1:30 Chairperson's Remarks

CLINICAL IMMUNOGENICITY STRATEGY

1:35 Design and Implementation of Clinical Immunogenicity Program
Meena Subramanyam, Ph.D., Vice President, Translational Sciences & Technology, Biogen Idec, Inc.
Using case studies this talk will highlight critical quality attributes that can potentially impact the PK/PD properties of the therapeutic, and discuss the value of non-clinical studies and phase I human studies to understand the immunogenicity of the therapeutic. It will also provide recommendations for when and how immunogenicity assessments should be made in the pivotal clinical trials and how to develop an analysis plan to study the impact of anti-drug antibodies on clinical end points.

GLOBAL REGULATORY CONCERNS

2:05 FDA Guidance on Immunogenicity Testing
Susan Kirshner, Ph.D., Associate Chief, Laboratory of Immunology, Therapeutic Proteins, Biotechnology, FDA
The US FDA published its Draft Guidance for Industry: Assay development for immunogenicity testing of therapeutic proteins in December 2009. The Draft Guidance provides FDA recommendations for the development and validation of assays

to test for anti-therapeutic antibodies to protein therapeutics. The Guidance has undergone a period of public comment and the Agency is currently assessing the comments provided by the public with the aim of revising the Draft Guidance. This talk will highlight aspects of the Draft Guidance.

2:35 European Update on Unwanted Immunogenicity of Biologicals and Biosimilars
Robin Thorpe, Ph.D., FRCPath, Head, Biotherapeutics Group, National Institute for Biological Standards and Control, UK
The Biosimilars Working Party of the CHMP has drafted a guideline on unwanted Immunogenicity Assessment of Biotechnology-Derived Therapeutic Proteins, and a new guideline on immunogenicity assessment of monoclonal antibodies intended for *in vivo* clinical use is being drafted. This presentation will provide an update on unwanted immunogenicity and the status and interpretation of existing EU guidelines. Considerations relevant to the immunogenicity assessment of biosimilars will also be included.

3:05 Networking Refreshment Break in the Exhibit Hall with Poster Viewing

3:35 Panel Discussion with the Speakers

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

ROLE OF T REGULATORY CELLS

4:05 Can Enhancement of T Regulatory Cell Function Decrease Immunogenicity?
Ethan M. Shevach, M.D., Chief, Cellular Immunology Section, Laboratory of Immunology, National Institute of Allergy and Infectious Diseases, National Institutes of Health
Studies over the past 15 years have identified a new lineage of T lymphocytes, T Regulatory Cells, that express the transcription factor Foxp3. Foxp3+ Treg are a dedicated population of suppressor T cells and function on multiple different target cell types within the immune system. Foxp3+ Treg cells use a variety of suppressor mechanisms including the secretion of suppressor cytokines. Enhancement of Treg function has been proposed as a novel method for the treatment of autoimmunity and transient activation of Treg may facilitate the induction of tolerance to both allografts and immunogenic proteins.

4:35 End of Plenary Session and Part One

PART TWO:

November 17-18

IMMUNOGENICITY PREDICTION AND MITIGATION

THURSDAY, NOVEMBER 17

4:45 BREAKOUT SESSIONS

Table 1: Sub-Visible Particles and Immunogenicity
Moderator: Nadine M. Ritter, Ph.D., Senior CMC Consultant, Biologics Consulting Group, Inc.

Table 2: How Predictive are the Methods to Analyze T Cell Epitopes?
Moderator: Matthew Baker, Ph.D., CSO, Antitope Ltd.

Table 3: Immune Tolerance Approaches
Moderator: David W. Scott, Ph.D., Professor and Vice Chair for Research, Department of Medicine, Uniformed Services University of Health Sciences, Bethesda

Table 4: What Does the FDA expect from an Immunogenicity Program
Moderator: Laura Salazar, CDER, FDA and Daniela Verthelyi, M.D., Ph.D., Chief, Laboratory of Immunology, Therapeutic Proteins, CDER, FDA

Table 5: Immunogenicity Lessons from the Literature
Moderator: Fiona A. Harding, Ph.D., Senior Principal Research Scientist, Biologics Technologies, Abbott Biotherapeutics Corp.

Table 6: Relevance of Animal Models for Predicting the Immunogenicity of Therapeutic Proteins
Moderator: Kristina Howard, D.V.M., Ph.D., FDA Commissioner's Fellow, Therapeutic Proteins, Pharmaceutical Sciences, CDER, FDA

5:45 – 7:00 Networking Reception in the Exhibit Hall

FRIDAY, NOVEMBER 18

FACTORS THAT CONTRIBUTE TO IMMUNOGENICITY

8:30 am Chairperson's Remarks
Matthew Baker, Ph.D., CSO, Antitope Ltd.

8:35 Immunogenicity, why, how and what?
Michel Awwad, Senior Director, PDM-NBE, Pfizer, Inc.

9:05 Tools, Tools, Tools and even more Tools! How to Predict Immunogenicity *in Silico*, *in Vitro* and *in Vivo* – an Overview
Melody Sauerborn. Ph.D., Pharmaceutical Sciences, University of Utrecht, and CEO, ADA InVivo BV
New analytical tools have been implemented in drug development processes to detect and characterize drug aggregates. Besides analytical tools, the industry uses biological tools such as *in silico*, *in vitro* and *in vivo* to predict immunogenicity of protein drugs. This presentation gives an overview about the currently used biological tools and discusses their pro and cons.

9:35 Coupling of Aggregation and Immunogenicity in Biotherapeutics: T- & B-Cell Immune Epitopes May Contain Aggregation Prone Regions
Sandeep Kumar, Ph.D., Principal Scientist, Biotherapeutics Pharmaceutical Sciences, Pfizer, Inc.
Aggregation and immunogenicity are among the major bottlenecks during discovery and development of biotherapeutics. Computational tools that can predict aggregation prone regions as well as T- & B-cell immune epitopes from protein sequence and structure have become available recently. In this talk I shall describe

a potential coupling between aggregation and immunogenicity: T-cell and B-cell immune epitopes in therapeutic proteins may contain aggregation prone regions. The details of biological mechanisms behind this observation remain to be understood. However, this observation opens up an exciting potential for rational design of de-immunized novel, as well as follow on, biotherapeutics with reduced aggregation propensity.

10:05 Identifying Immunogenic Regions of Antibodies
Fiona A. Harding, Ph.D., Senior Principal Research Scientist, Biologics Technologies, Abbott Biotherapeutics Corp.
Humanized and fully human antibodies can induce unwanted immune responses *in vivo*. The identification and modification of epitope regions of antibodies to create risk-reduced candidates will be discussed.

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

MEASURES TO AVOID IMMUNOGENICITY

11:10 Advances in Abrogating Immunogenicity with Fc Fusion Proteins
David W. Scott, Ph.D., Professor & Vice Chair, Research, Department of Medicine, Uniformed Services, University of Health Sciences, Bethesda
Therapeutic proteins have the potential to elicit immune responses that can limit their efficacy. Understanding how to reverse and/or prevent this immunogenicity will be the focus of this presentation. Tolerance induction using IgG and Fc conjugated fusion proteins has been studied for over three decades. This talk will explore the basis of this tolerogenicity and its application using different modes of presentation to the immune system. The mapping and recognition of potentially tolerogenic peptides in therapeutic proteins will be emphasized. Possible mechanisms for their success and applications for the future will be discussed.

11:40 New Data on the Impact of T Epitope Removal on Immunogenicity and Aggregate Formation
Matthew Baker, Ph.D., CSO, Antitope Ltd.
The importance of T cell help in the development of anti-drug antibodies has been generally accepted and there are numerous *in silico*, *in vitro* and *in vivo* technologies that attempt to measure and quantify T cell epitopes. The focus of this presentation will be to provide case study examples of how some of these technologies can be applied to select protein therapeutics with a reduced risk of immunogenicity. Furthermore new data will be presented on how aggregates in some formulations can trigger innate responses that ultimately enhance T cell immunogenicity *in vitro*.

12:10 pm Lunch on Your Own

IMPACT OF SUB-VISIBLE PARTICLES ON IMMUNOGENICITY

1:30 Chairperson's Remarks
Nadine Ritter, Ph.D., Senior CMC Consultant, Biologics Consulting Group, Inc.

» KEYNOTE PRESENTATION

1:35 Innate Immune Response Modulating Impurities

Daniela Verthelyi, M.D., Ph.D., Chief, Laboratory of Immunology, Therapeutic Proteins, CDER, FDA
Immune cells express numerous receptors that respond to conserved molecular patterns present in pathogens as well as in stressed tissues. This talk will review recent data, present a few cases, and discuss the role of trace levels of impurities in therapeutic proteins that stimulate the innate immune response in facilitating an immunogenic response to therapeutic proteins.

2:05 Sub-Visible Particles Relating to Pre-Clinical Immunogenicity Risk Assessment and Clinical Outcome
Mary Cromwell, Ph.D., Senior Scientist & Associate Director, Protein Analytical Chemistry, Genentech, Inc.

2:35 Studies from Utrecht/Leiden University on Impact of Aggregates on Immunogenicity in Immune Tolerant Mice
*Miranda van Beers, Ph.D., Research Scientist, Analytics, Bioprocessing Technology Institute, A*STAR*
The clinical immunogenicity of therapeutic proteins is often associated with the presence of aggregates. However, insight in what types of aggregates cause immunogenicity is lacking. Immune tolerant mice help to understand the mechanism responsible for breaking tolerance. This talk will review data on the immunogenicity of aggregates with different physicochemical characteristics in immune tolerant mice. The immune response against oxidized protein and protein adsorbed on (sub)visible particles will be discussed.

3:05 Networking Refreshment Break in the Exhibit Hall with Poster Viewing

3:30 Recommended Strategies for the Assessment of Protein Aggregates in Pharmaceutical Biotech Product Development
John den Engelsman, Ph.D., Analytical Development and Validation, Merck, Sharpe & Dohme
Within the European Immunogenicity Platform (EIP) (http://www.e-i-p.eu), the Protein Characterization Subcommittee (EIP-PCS) has been established to discuss and exchange experience of protein characterization in relation to immunogenicity. As representatives of EIP-PCS, we reviewed the current state of methods for analysis of protein aggregates. Moreover, we elaborate on why these methods should be used during product development and make recommendations to the biotech community with regard to strategies for their application during the development of protein therapeutics.

4:00 Recent Developments Concerning Sub Visible Particulate (SVP) Characterization for Biotech Products
Nadine M. Ritter, Ph.D., Senior CMC Consultant, Biologics Consulting Group, Inc.
Protein-based therapeutics require orthogonal analytical methods for product characterization and comparability, many of which focus on product- and process-related impurities. One evolving concern is the characterization and quantitation of SVPs. Current compendial methods and specification limits were designed for extraneous particulate matter. But the emergence of biotechnology products has shown that SVPs are often intrinsic product-related material, challenging the available technology. It also may require safety limits different from those for extrinsic SVPs. This talk will provide an overview of the current expectations for the characterization and quantitation of SVPs in biotechnology products.

4:30 End of Part Two

Pricing and Registration Information

PRE-CONFERENCE SHORT COURSES

	Commercial	Academic, Government, Hospital-affiliated
One short course	$695	$395
Two short courses	$995	$695

November 15	
SC1: Technical Advice on Assay Development, Validation and Sample Analysis	SC2: Development of Neutralizing Antibody Assays

CONFERENCE PRICING

Summit Pricing - Best Value (Includes access to both conferences)

Early Registration Discount until August 26	$2290	$935
Advance Registration Discount until October 7	$2450	$1025
Registrations after October 7 and on-site	$2595	$1095

Individual Conference Pricing

Early Registration Discount until August 26	$1395	$695
Advance Registration Discount until October 7	$1545	$775
Registrations after October 7 and on-site	$1745	$895

November 16-17	November 17-18
Part 1: Immunogenicity Assessment and Clinical Relevance	Part 2: Immunogenicity Prediction and Mitigation

CONFERENCE DISCOUNTS

Poster Submission-Discount ($50 Off)
Poster abstracts are due by October 21, 2011. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact jring@healthtech.com. *CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

REGISTER 3 - 4th IS FREE: Individuals must register for the same conference or conference combination and submit completed registrationform together for discount to apply.

Additional discounts are available for multiple attendees from the same organization. For more information on group rates contact David Cunningham at +1-781-972-5472

ADDITIONAL REGISTRATION DETAILS

Each registration includes all conference sessions, posters and exhibits, food functions, and access to the conference proceedings link.

Handicapped Equal Access: In accordance with the ADA, Cambridge Healthtech Institute is pleased to arrange special accommodations for attendees with special needs. All requests for such assistance must be submitted in writing to CHI at least 30 days prior to the start of the meeting.

To view our Substitutions/ Cancellations Policy, go to http://www.healthtech.com/regdetails

Video and or audio recording of any kind is prohibited onsite at all CHI events.

If you are unable to attend but would like to purchase the Immunogenicity Summit conference CD for $350 (plus shipping), please visit ImmunogenicitySummit.com. Massachusetts delivery will include sales tax.

How to Register: **ImmunogenicitySummit.com**

reg@healthtech.com • P: 781.972.5400 or Toll-free in the U.S. 888.999.6288

Please use keycode **IMN F** when registering!

Please refer to the Registration Code below:

Cambridge Healthtech Institute
250 First Avenue, Suite 300, Needham, MA 02494
www.healthtech.com • Fax: 781-972-5425