Final Agenda

October 10-12, 2012
DoubleTree by Hilton Hotel ■ Bethesda, Maryland

Fourth Annual Immunogenicity Summit 2012

Register by September 14 & SAVE UP TO $200!

The Leading Event Connecting Industry, Academia and Regulators on Immunogenicity Testing, Immunogenicity Avoidance and Regulatory Guidance

PART ONE: OCTOBER 10-11
Immunogenicity Assessment and Clinical Relevance

PART TWO: OCTOBER 11-12
Immunogenicity Prediction and Mitigation

Pre-Conference Short Courses

OCTOBER 9

SC1: Assays for Measuring Binding Antibodies

SC2: Neutralizing Antibody Assays

SC3: Navigating the Regulatory Hierarchy of Concerns to Minimize Impact of Immunogenicity-Related Risks on Product Registration

Keynote Speakers

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

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

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Cambridge Healthtech Institute

Fourth Annual

Immunogenicity Summit 2012

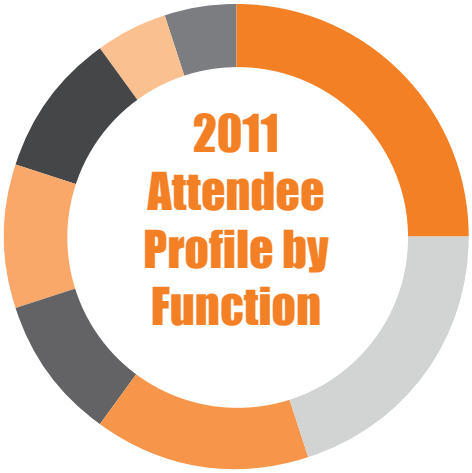
Overview

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

Following year-on-year success, our fourth Immunogenicity Summit will continue to provide strong interaction and discussion with the regulatory authorities (40 FDA representatives in 2011), updates on immunogenicity testing, pre-clinical and clinical strategies, and factors that contribute to immunogenicity including aggregates and sub-visible particles.

New this year will be a strong focus on the impact of immunogenicity on PKPD, the relationship between immune complexes and immunogenicity, immunogenicity for biosimilars, predictive methods for immunogenicity, and immune tolerance approaches.

The Leading Summit Connecting Industry, Academia and Regulators on Immunogenicity Testing, Immunogenicity Avoidance and Regulatory Guidance



Who Will Attend

Directors, Team Leaders, Project Managers, Heads, Senior Scientists, Principal Scientists, Research Scientists, Research Associates, and Managers working at Pharmaceutical, Biotechnology and Academic/Government Organizations and working in:

- Immunogenicity
- Immunology
- Biotherapeutics
- Monoclonal Antibodies
- Clinical Pharmacology
- Immunotoxicology
- Immunoassay
- Medical Affairs
- Drug Safety
- Clinical Testing
- Bioanalytical Sciences
- Infectious Diseases
- Protein Analysis
- External Scientific Affairs
- Bioanalysis
- Assay Development
- Biomarkers
- Pre-Clinical and Clinical Development
- Clinical Affairs
- R&D
- Regulatory Affairs
- PKPD

SC 1: Assays for Measuring Binding Antibodies*

8:00-9:00 am Short Course Registration

9:00-12:00 pm Short Course

Course Instructors:
Deborah Finco, Ph.D., Senior Principal Scientist, Immunotoxicology COE, Pfizer, Inc.
Stephen Keller, Ph.D., Associate Director II, Pre-Clinical & Clinical Development Sciences, GPRD Abbott Biotherapeutics Corp.

This interactive session will enable attendees to work out an immunogenicity pre-clinical and clinical testing strategy for various molecules including bi-functional and other novel scaffolds. Recent advances will be presented and areas of difficulty will be addressed 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. This course is of intermediate level.

The following topics will be covered:

- Strategies for assay design
- Assay methodologies and various technologies
- Other considerations
- Critical considerations in assay validation and areas of controversy
- Common problems (matrix interferences, pre-existing antibodies)
- Data

SC 2: Neutralizing Antibody Assays*

12:30-1:30 pm Short Course Registration

1:30-4:30 pm Short Course

Course Instructors:
Deborah Finco, Ph.D., Senior Principal Scientist, Immunotoxicology COE, Pfizer, Inc.
Stephen Keller, Ph.D., Associate Director II, Pre-Clinical & Clinical Development Sciences, GPRD Abbott Biotherapeutics Corp.

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 understand how to design, develop and validate their assays for neutralizing antibodies with discussion on competitive ligand binding vs. bioassay formats. This discussion will include troubleshooting and case studies with actual compounds. Attendees are encouraged to contribute with their own experiences and to bring questions for discussion or submit to the meeting organizers in advance. This course is of intermediate level.

The following topics will be covered:

- Strategy for design, development and validation of neutralizing antibody assays
- Challenges and approaches to resolve commonly encountered issues
- Interpretation and application of results
- Emerging trends in the development of neutralizing antibody assays
- Clinical implementation of established neutralizing antibody assays
- Regulatory guidance and guidelines

Dinner SC 3: Navigating the Regulatory Hierarchy of Concerns to Minimize the Impact of Immunogenicity-Related Risks on Product Registration*

4:30-5:30 pm Short Course Registration

5:30-8:30 pm Short Course

Course Instructors:
Paul Chamberlain, NDA Advisory Board
Amy Rosenberg, M.D., Director, Therapeutic Proteins, CDER/FDA

The following topics will be covered:

1. Priorities for the regulator

- Hierarchy of concerns
- Data requirements
- Common gaps

2. Integrated approach

- Risk identification
- Aligning identified risks with CMC, bioanalytical, non-clinical and clinical strategy
- Ongoing risk management

3. Interactive case study

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

**Separate registration required*

PART ONE:
Immunogenicity Assessment and Clinical Relevance

WEDNESDAY, OCTOBER 10

7:30 am Registration and Morning Coffee

8:30 Chairperson's Opening Remarks
Josi Holz, M.D., CMO, Ablynx NV

CHALLENGES OF IMMUNOGENICITY ASSAYS

8:35 Drug Interference in Neutralizing Antibody Assays: Attempts at Overcoming the Challenge
Marie T. Rock, Ph.D., Vice President, Protein Bioanalysis, Midwest BioResearch LLC, a Wil Research Company
In order to fully characterize and gain an understanding of the nature of the immune response a cascade of analytical methods are used in a stepwise sequence. The final assessment involves the evaluation of the possible neutralizing activity of anti-drug antibodies that may be present. Generally these assays are cell based methods that respond to the biological activity of the drug. As a result they tend to be less sensitive than the typical immunogenicity panel of methods, but more importantly they are far more susceptible to drug interference. These drug effects will be demonstrated using case studies to show some possible approaches to minimize the impact of circulating drug.

9:05 Different Technology Platforms that Address Challenges Faced for the Development of Fit for Purpose Immunogenicity Assays
Maureen Deehan, Ph.D., Head, Pharmacology, Experimental Science & Translational Medicine, NovImmune SA
There are multiple formats available for anti-drug antibody assays. Thus, precision, accuracy, propensity for drug/target interference, cost of reagents and assay throughput must be considered when choosing a format. A case study involving a therapeutic antibody and comparison of results from different formats will be presented. Also work within the framework of the European Immunogenicity Platform will be discussed.

9:35 Impact of Analytical and Biological Variability on Observed Outcomes from Tiered Immunogenicity Assays
Robert J. Kubiak, Ph.D., Research, Translational Sciences, MedImmune LLC
Insufficient evaluation of inherent analytical variability of an immunogenicity assay in context of biological variability of the target population as well as neglecting to take into account relationships between the screening and confirmatory cut points may lead to significant differences between the expected and observed positive rates from tiered analyses of samples from drug-naive patients. This talk will discuss how analytical variability impacts selection of screen and confirmatory cut points and affects the overall outcomes from tiered immunogenicity assays.

10:05 Talk Title and Speaker to be Announced

Sponsored by Thermo SCIENTIFIC

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

DETECTION OF IMMUNE COMPLEXES

KEYNOTE PRESENTATION

11:15 Detection of Immune Complex Formation in Non-Clinical Studies and Implications for Clinical Risk Assessment
Steve J. Swanson, Ph.D., Executive Director, Medical Sciences, Clinical Immunology, Amgen, Inc.
When human therapeutics are used in non-clinical studies it is anticipated that the animals will mount a robust immune response. This immune response can result in a high concentration of circulating anti-therapeutic protein antibodies. When large doses of the protein therapeutic are administered, especially via the intravenous route, there is a potential for large immune complexes to rapidly form. Detecting these immune complexes can be challenging but is important in order to understand pathology findings in the animals.

11:45 Impact of a Pre-Clinical Generic ADA Assay Detecting Drug-ADA Immune Complexes on Drug-Development Programs
Priya Sriraman, Ph.D., Principal Scientist, DMPK, F. Hoffmann-La Roche
Evaluation of immunogenicity in pre-clinical toxicological studies is an integral part of biotherapeutics development programs. Animals being evaluated for toxicology have high levels of circulating drug. We describe a highly drug tolerant, generic ADA assay and its impact on understanding toxicological findings and active drug exposure. Three case studies will be presented spanning monoclonal antibody therapeutics as well as a non-mAb protein therapeutic, and cynomolgus monkey and rat as toxicological species.

12:15 pm Immunogenicity in Biotherapeutic Development

Sponsored by COVANCE

Murty Chengalvala, Ph.D., Program Director, Senior Scientist, Immunology Services, Covance
The potential immunogenicity of biotherapeutics is a high profile safety concern for industry and regulatory authorities. As a CRO that amasses experience with a wide variety of biologics and clients' needs, Covance has unique vantage point on this topic. Various strategies for reagent generation and assay development will be discussed.

12:30 Title to be Announced

Sponsored by Thermo SCIENTIFIC

Jörgen Dahlström, Ph.D., MBA, Scientific Director, ImmunoDiagnostics, Thermo Fisher Scientific

12:45 Luncheon Presentation *(Opportunity available, please contact Tim McLucas, tmclucas@healthtech.com)*

CLINICAL RELEVANCE OF ANTI-DRUG ANTIBODIES

2:15 Chairperson's Remarks
Steven J. Swanson, Ph.D., Executive Director, Medical Sciences, Clinical Immunology, Amgen, Inc.

FEATURED PRESENTATION

2:20 Relevance of A nimal Models for Predicting the Immunogenicity of Therapeutic Proteins
Jack Ragheb, M.D., Ph.D., Principal Investigator, Immunology, Therapeutic Proteins, CDER/FDA
"Humanized" mice that fully recapitulate the human hematopoietic system may permit direct *in vivo* assessment of human immunogenicity to a therapeutic protein. This session will describe the nature, limitations, utility, and predictive value of *in vitro* and *in vivo* model systems. Case studies will illustrate how pre-clinical data and a risk-based assessment may help inform the probability of immunogenicity in humans.

2:50 Correlating ADA Data with Effects on PK, PD, Safety and Efficacy
Stephen Keller, Ph.D., Associate Director II, Pre-Clinical & Clinical Development Sciences, GPRD Abbott Biotherapeutics Corp.
The development of anti-drug antibodies can have consequences in patients that range from relatively benign to (rarely) very serious. Establishing the clinical, pharmacokinetic, and pharmacologic relevance of ADA development in patients is a worthwhile line of investigation in many circumstances. But is this something that should be done routinely? If so, what's the best way to analyze data to explore these relationships? This presentation will use case studies to highlight some of the history, techniques, and outcomes of investigations into the effects of ADA on PK, PD, safety, and efficacy of biotherapeutics.

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

4:00 Immunogenicity: A Case Study from Pre-Clinical to Clinical
Deborah Finco, Ph.D., Immunotoxicology COE, Pfizer, Inc.

4:30-5:30 In-Depth Breakout Discussions

Table 1: Challenges in Developing Neutralizing Antibody Assays
Moderator: Deborah Finco, Ph.D., Senior Principal Scientist, Immunotoxicology COE, Pfizer, Inc.

Table 2: Dealing with Pre-Existing Positive ADA Activity in Study Patients
Moderator: Jim McNally, Ph.D., Senior Principal Scientist, Pfizer, Inc.

Table 3: Practical Application of Immunogenicity Pre-Clinical Risk Assessment
Moderator: Paul Chamberlain, NDA Advisory Board

Table 4: Detection of Immune Complexes and Their Impact on Immunogenicity Assessment
Moderator: Steve J. Swanson, Ph.D., Executive Director, Medical Sciences, Clinical Immunology, Amgen, Inc.

Table 5: Immunogenicity Testing During Clinical Trials
Moderator: Frank F. Weichold, M.D., Ph.D., Director, Clinical Pharmacology and DMPK, Translational Science, MedImmune, LLC

Table 6: IgE Anti-Drug Assay Development and Validation
Moderator: Jörgen Dahlström, Ph.D., MBA, Scientific Director, ImmunoDiagnostics, Thermo Fisher Scientific

Table 7: Relevance of Animal Models for Predicting the Immunogenicity of Therapeutic Proteins
Moderator: Jack Ragheb, M.D., Ph.D., Principal Investigator, Immunology, Therapeutic Proteins, CDER/FDA

5:30-6:30 Welcome Reception in the Exhibit Hall with Poster Viewing

6:30 End of Day One of Immunogenicity Assessment and Clinical Relevance

THURSDAY, OCTOBER 11

7:30-8:15 am Sponsored Breakfast Presentation Available
(Opportunity available, please contact Tim McLucas, tmclucas@healthtech.com)

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

CLINICAL IMMUNOGENICITY TESTING STRATEGY

8:35 Clinical Trial Strategy and Immunogenicity Assessment for a Novel Protein Therapeutic
Josi Holz, M.D., CMO, Ablynx NV
This talk will provide an introduction to the Nanobody technology platform and outline the non-clinical development and immunogenicity risk assessment program together with the clinical strategy and the immunogenicity risk management. Experiences with the Regulatory Authorities will be presented.

9:05 Pre-Existing Reactivity and Risk Mitigation
Jim McNally, Ph.D., Senior Principal Scientist, Pfizer, Inc.
The increased frequency of pre-existing reactivity to biotherapeutics during clinical assay development have led us to implement a risk mitigation plan that relies upon early

identification of protein modalities more likely to be targeted by pre-existing reactivity and disease indications more likely to manifest these reactivities.

BIOSIMILARS

FEATURED PRESENTATION

9:35 Fundamental Considerations for Defining "Comparable" Immunogenicity of Biosimilar Therapeutic Monoclonal Antibodies

Paul Chamberlain, NDA Advisory Board

This presentation will reflect on methodological limitations for interpretation of relative Immunogenicity of biosimilar and reference therapeutic monoclonal antibodies, in emphasizing the relevance of correlation of bioanalytical signals with appropriate clinical endpoints and the possible need for post-marketing observational studies to indicate the impact of detected differences in anti-drug antibody (ADA) incidence and magnitude on sustainability of treatment benefit. Arguably, there can be no pre-defined margin of difference based on incidence and magnitude of detected ADA's.

10:05 Immunogenicity Assessment Using Novel ELISA Alternative Detection Technologies

Sponsored by PerkinElmer For the Better

Martin Boissonneault, Senior Scientist, PerkinElmer Life Science and Technologies

Biotherapeutics often elicit immune responses and clinical consequences of anti-drug antibodies (ADA) can result in adverse events. The presence of ADA is a safety concern and must be evaluated and correlated with pharmacological or toxicological observations. The development of rapid, sensitive assays for ADA detection is essential. AlphaLISA and DELFIA assays used to detect ADA in serum samples can detect ADA in the low ng/mL range, maintain excellent performance in serum and exhibit high drug tolerance.

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

FEATURED PRESENTATION

11:10 Immunogenicity Considerations in the Approval of Generic Enoxaparin in the US

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

Enoxaparin belongs to a class of drugs known as low molecular weight heparins (LMWH). These products can form complexes *in vivo* with chemokine PF4 and elicit immune responses that have been linked to a serious adverse effect: heparin induced thrombocytopenia. Approval of generic enoxaparin required establishing bioequivalence of the API as well as assessing the risk that the generic enoxaparin product would pose a greater risk of immunogenicity.

11:40 Immunogenicity Assessment of Biosimilars: Fit For Purpose Strategy with Totality of Evidence

Patrick Liu, M.D., Ph.D., Global Head, Bioanalytical Sciences and Technologies, Teva Pharmaceutical Industries, Ltd.

Immunogenicity testing has become one of the most critical considerations for the development of therapeutic biologics. This presentation will provide an overview of technology and methodology issues and challenges for biosimilars and advice on a fit-for-purpose immunogenicity assessment program, discuss totality of evidence and immunogenicity data interpretation, and examine immunogenicity comparability of biosimilars.

12:10 pm Luncheon Presentation *(Opportunity available, please contact Tim McLucas, tmclucas@healthtech.com)* **or Lunch on Your Own**

12:30 Registration for Part Two: Immunogenicity Prediction and Mitigation

COMBINED PLENARY SESSION: Parts One and Two

1:30 Chairperson's Remarks

Valerie Quarmby, Ph.D., Director and Principal Scientist, BioAnalytical Sciences, Genentech, Inc.

ADVANCES IN OUR UNDERSTANDING OF IMMUNOGENICITY

FEATURED PRESENTATION

1:35 Antibody/Antigen Complexes: Structure, Presentation & Immunogenicity

Roy Jefferis, Ph.D., C.Chem., FRSC, MRCP, FRCPath, D.Sc., Professor Emeritus, School of Immunity & Infection, University of Birmingham UK

It is accepted that aggregated forms of recombinant proteins can stimulate an immune response with the development of anti-drug antibodies (ADA). However, administered antibody, in the absence of aggregates, forms immune complexes that can be similarly processed. Complexes binding to Fc and complement receptors ((FcγR, FcRn, CR) can be directed to cellular compartments that process antigen for presentation and hence ADA generation. Protocols inducing tolerance may circumvent the development of ADA.

2:05 Interaction of Aggregrated Protein Therapeutics with Dendritic Cells and the Enhanced Activation of T Cells

Matthew Baker, Ph.D., CSO, Antitope Ltd

The importance of T cell help in the development of anti-drug antibodies has been widely accepted as a significant risk factor. New data will be presented showing how protein aggregates can trigger innate responses leading to distinct dendritic cell phenotypes. Data from recent studies highlighting the impact of aggregates with specific properties on drug immunogenicity will also be discussed.

COMBINED PLENARY SESSION: Parts One and Two

UPDATE ON REGULATORY GUIDANCE

FEATURED PRESENTATION

2:35 Update on US Regulatory Guidance

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

Treatment of patients with therapeutic proteins invariably results in the development of anti-drug antibodies in some of those patients. Anti-drug antibodies may negatively impact patients by inhibiting the activity of endogenous counterparts, reducing efficacy, altering pharmacokinetics and leading to hypersensitivity reactions. Anti-drug antibodies should be assessed during clinical studies and risk based mitigation strategies incorporated into clinical study designs. This talk will cover FDA guidance on these topics.

3:05 PANEL DISCUSSION: Regulatory Expectations Regarding Immunogenicity Assessment

Panelists include:
Susan Kirshner, Ph.D., Associate Chief, Laboratory of Immunology, Therapeutic Proteins, Biotechnology, CDER/FDA
Paul Chamberlain, NDA Advisory Board

- How and when to approach the regulators: Benefits of discussion with the regulators
- How much characterization is necessary? How much is too much? What is the essential strategy?
- Proper validation and characterization of assays
- Neutralizing antibody assays: When should they be carried out and why?
- Ligand binding assays. Can they be used instead of cell-based assays?
- Pitfalls to avoid

3:35 End of Plenary Session and Part One

3:35- 4:00 Refreshment Break in the Exhibit Hall with Poster Viewing, Followed by Part Two

PART TWO:
Immunogenicity Prediction and Mitigation

4:00 Chairperson's Opening Remarks

Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.

FACTORS CONTRIBUTING TO IMMUNOGENICITY

4:05 Subvisible Particles in Protein Therapeutics and Immunogenicity: Is There a Link?

Wim Jiskoot, Ph.D., Professor, Division of Drug Delivery Technology, Leiden University

Practically all protein therapeutics are immunogenic and contain subvisible particles (SVPs). Although it is tempting to assume a correlation, our current understanding about the contribution of SVPs to protein immunogenicity is still limited. In this presentation I will address the following question related to the presence of SVPs in protein therapeutics: where do they come from; what is their nature; how can we characterize and quantify them; which tools do we have to assess their contribution to unwanted protein immunogenicity?

4:35 Photooxidation-Enhanced Immunogenicity

Theodore W. Randolph, Ph.D., Gillespie Professor of Bioengineering, Chemical and Biological Engineering, University of Colorado

During manufacture, therapeutic proteins may be exposed to ultraviolet (UV) radiation which may cause photooxidative damage, which in turn could lead to physical changes such as aggregation and enhanced immunogenicity. We exposed murine growth hormone (mGH) to controlled doses of UV radiation, and examined the resulting chemical, physical and immunogenic changes in the protein. When administered subcutaneously to mice, UV-irradiated mGH provoked T-cell dependent immune responses, but no immunological memory. mGH immunogenicity increased with increasing UV radiation doses.

Sponsored by The Jackson Laboratory

5:05 Reconstitution of the Human Immune System in Mice: Utility in Preclinical Research

Leon L. Hall, Ph.D., Director, Scientific Operations, in vivo Pharmacology Services, The Jackson Laboratory

Drug discovery research requires predictive animal models that can better mimic human biology. Immunodeficient mice engrafted with a human immune system enable scientists to study human biological processes in vivo without putting patients at risk. The mice with an engrafted human immune system represent one form of humanized mouse models and leverage the severely immunodeficient mouse strain, NOD scid IL2 receptor gamma chain knockout mice (NSG) which readily supports the engraftment and multi-lineage differentiation of human hematopoietic stem cells. This presentation will discuss various methodologies to establish engraftment, functional characterization of the reconstituted human immune system andresearch applications in a broad range of therapeutic areas such as infectious disease, hematopoiesis, stem cell differentiation and autoimmune disorders. Preliminary data on immunogenicity testing of protein drugs in the humanized mice will also be discussed.

5:35 Working Towards Building a "Value Added Proposition" for Immunogenicity Prediction and Risk Management

Manoj Rajadhyaksha, Ph.D., Director, Bioanalytical Sciences, Regeneron, Inc.

The immunogenicity profile of a biotherapeutic is determined by a multiplicity of factors ranging from product related, patient (host) related, bioanalytical to process or manufacturing related factors. This creates a complex situation that does not allow direct correlation of such risk factors to the observed incidence of immunogenicity. Therefore, a mechanistic understanding of how these risk factors individually or in concert influence the overall incidence and risk of immunogenicity is crucial to design the best benefit/risk profile for a given biotherapeutic in a given indication.

6:05-7:00 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 End of Day One of Immunogenicity Prediction and Mitigation

FRIDAY, OCTOBER 12

8:30 am Chairperson's Remarks

Wim Jiskoot, Ph.D., Professor, Division of Drug Delivery Technology, Leiden University

PREDICTIVE METHODS FOR IMMUNOGENICITY

8:35 Predictive Immunogenicity Assessment Strategies to Reduce Immunogenicity Risk to Biotherapeutics

Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen, Inc.

The therapeutic development process often involves evaluation of several key attributes, such as potency, safety, PK/PD, molecule manufacturability and immunogenicity. Since bio-therapeutics may elicit an immune response when administered in animals and humans, applying a quality by design immunogenicity assessment strategy during early therapeutic optimization can minimize immunogenicity associated risks. This study summarizes data generated using *in silico*, *in vitro* and *in vivo* immunogenicity related analytical tools utilized to support therapeutic development.

FEATURED PRESENTATION

9:05 *In vitro* Prediction Technologies for Immunogenicity Assessment

Valerie Quarmby, Ph.D., Director and Principal Scientist, BioAnalytical Sciences, Genentech, Inc.

This talk will discuss unwanted immune responses to biologics, and review what immunogenicity risk assessment tools, technologies and data sets may be deployed to enable informed decision making during biotherapeutics product and process development. The talk will also discuss recent data from selected *in vitro* models and highlight "gaps" where there may be opportunities to even further develop/refine such tools and technologies.

9:35 Case Studies Showing How T Cell Epitope Analysis Can be Used as a Basis for the Design of the Clinical Immunogenicity Program

Timothy Hickling, Ph.D., Associate Research Fellow, PDM Immunogenicity Sciences, Pfizer, Inc.

Several tools exist for characterizing T cell epitopes, from in silico prediction, through *in vitro* characterization to direct *in vivo* validation. The helper T cells themselves are crucial in driving immunoglobulin class switching and strong anti-drug antibody responses, leading to the possibility that the quantification of T cell epitopes could relate directly to the incidence of clinical immunogenicity. A selection of case studies relating T cell epitope assessments and clinical incidence of ADA will be presented. Understanding of clinically relevant T cell responses, through clinical quantification and HLA typing, could direct re-engineering of novel biotherapeutics to reduce immunogenicity risk.

10:05 Advances in Tools for Managing Immunogenicity Risk: How an Integrated Approach Can Help

Sponsored by PROIMMUNE www.proimmune.com

Nikolai Schwabe, Ph.D., CEO, ProImmune Limited

ProImmune has developed a comprehensive suite of *in vitro* assays to characterize immune responses against biological drugs. Assays that characterize DC, T cell and B cell responses can be combined to provide a comprehensive picture of the antigenicity of a therapeutic protein. The data from these assays enable well-informed design or selection of lead candidates, and can give a better understanding of the mechanisms underlying observed immunogenicity

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

IMMUNE TOLERANCE APPROACHES/REDUCING IMMUNOGENICITY

11:40 Reducing the Immunogenicity of Recombinant Immunotoxins by Identifying and Removing T Cell Epitopes

Mazor Ronit, M.Sc., Laboratory of Ira Pastan, Molecular Biology, NIH

Moxetumomab pasudotox and SS1P are immunotoxins that have been developed in our lab to treat cancer. In order to identify and eliminate T-cell epitopes, we used an *in vitro* expansion step which specifically expands T-cell populations that are reactive to naturally processed peptide, followed by ELISpot. This strategy had a 100% response rate which correlates with the immunogenicity response rate of patients with solid tumors that have been treated with the immunotoxin. We identified one highly-reactive and immunodominant epitope that stood out among multiple subdominant epitopes and constructed mutant RITs that retained sufficient protein expression, stability, activity, and had reduced T-cell immunogenicity.

12:10-1:00 pm In-Depth Breakout Discussions

Table 1: Product-Related Factors that Contribute to Immunogenicity

Moderator: Wim Jiskoot, Ph.D., Professor, Division of Drug Delivery Technology, Leiden University

Table 2: To what Extent can Immunogenicity Prediction Affect the Clinical Strategy?

Moderator: Timothy Hickling, Ph.D., Associate Research Fellow, PDM Immunogenicity Sciences, Pfizer, Inc.

Table 3: Immune Tolerance Approaches

Moderator: Amy Rosenberg, M.D., Director, Therapeutic Proteins, CDER/FDA

Table 4: Prediction Technologies for Immunogenicity

Moderator: Valerie Quarmby, Ph.D., Director and Principal Scientist, BioAnalytical Sciences, Genentech, Inc.

1:00 Luncheon Presentation *(Opportunity available, please contact Tim McLucas, tmclucas@healthtech.com)* **or Lunch on Your Own**

2:00 Chairperson's Remarks

Paul Chamberlain, NDA Advisory Board

KEYNOTE PRESENTATION

2:05 Immune Tolerance Induction: Novel Approaches for Novel Clinical Indications

Amy S. Rosenberg, M.D., Director, Division of Therapeutic Proteins, CDER/FDA

The choice of the tolerance induction regimen must consider the following: the appropriate regimen for the level of risk posed by the immune response; and the rapidity with which treatment for the underlying disease must be initiated. Thus, the need for expedient commencement of therapy for the underlying disease may restrict tolerance protocols to those which are less specific and more hazardous as regards infectious risk. This seminar will explore these various considerations in tolerance induction approaches focusing on novel approaches and novel clinical indications.

2:35 Peptides that Act as T Regulators: Implications for Control of Immunogenicity and Application to Protein Therapeutics

Annie de Groot, Ph.D., Director, Institute for Immunology & Informatics, University of Rhode Island

Immune responses to protein therapeutics and contaminating host cell proteins (HCP) can diminish drug safety and efficacy. This presentation addresses the critical role of T cell immunogenicity in early events leading to anti-drug antibody production. Effector T cell responses enhance anti-drug antibodies (ADA) while Regulatory T cell responses can suppress them. Case studies of epitope modification and tolerance induction to reduce immunogenicity risk, as well as potential immunogenicity of HCP contaminants, will be presented.

3:05 Lipid Mediated Induction of Immunological Ignorance/Tolerance

Sathy Balu-Iyer, Ph.D., Associate Professor, Pharmaceutical Sciences, SUNY-University at Buffalo

Immunogenic responses against therapeutic proteins are a major clinical complication that greatly impact safety and efficacy of protein based therapies. The talk focuses on lipid mediated Induction of immunological tolerance/ignorance. The pre-clinical studies showed that immunization with protein- phosphatidylserine complex lead to hypo-responsiveness towards therapeutic protein and this hypo-responsiveness could be adoptively transferred to a recipient mouse. Based on this novel finding, a reverse vaccination strategy is proposed as clinical intervention to mitigate immunogenicity of therapeutic proteins.

3:35 PANEL DISCUSSION: Risk Assessment and Risk Management

Panelists include:

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

Additional Panellists to be Announced

Timothy Hickling, Ph.D., Associate Research Fellow, PDM Immunogenicity Sciences, Pfizer, Inc.

- Management in the clinic of products with low and high risk of immunogenicity related adverse events
- Investigative approaches to consider when only a sub population mounts immune responses to a therapeutic protein product
- Immunogenicity risk assessment as a function of the clinical condition: acute, chronic, malignant, autoimmune etc.
- Features of a good risk analysis and risk mitigation plan
- Sharing of experiences of applying risk assessment in pre-clinical and clinical studies

4:00 End of Conference

TRACK HOP: CO-LOCATED EVENT

Register for the Immunogenicity Summit and gain access to the concurrent PK/PD of Novel Constructs conference

Inaugural

PK/PD of Novel Constructs

Bispecific Antibodies, Antibody Fragments, and ADCs

October 10-12, 2012

This conference will delve into tools for understanding the *in vivo* activity of novel constructs in animal models and clinical studies. It will highlight engineering approaches for optimal efficacy, safety and metabolism.

Hotel and Travel Information

Conference Venue and Hotel:

DoubleTree by Hilton Hotel
8120 Wisconsin Avenue
Bethesda, MD 20814
Tel: 301-652-2000
Discounted Room Rate: $225 s/d
Discounted Reservation Cut-off Date: September 12, 2012

Please visit our website to make your reservations online, or call the hotel directly to reserve your sleeping accommodations. You will need to identify yourself as a Cambridge Healthtech Institute conference attendee to receive the discounted room rate with the host hotel. 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.

Flight Discounts:

Special discounts have been established with American Airlines. Please use one of the following methods:

- Call American Airlines 1-800-433-1790 and use Conference code 13H2BN
- Go to www.aa.com/group enter 13H2BN in the promotion discount box
- Contact our dedicated travel agent, Wendy Levine at 1-877-559-5549 or wendy.levine@protravelinc.com

Car Rental Discounts:

Special rental discounts have been established with Hertz for this conference.

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- Call Hertz at 1-800-654-3131 and use our Hertz Convention Number (CV):04KL0003

Delegate Testimonials

"Program and participants were first class."
- Senior Scientist, Novo Nordisk

"The round tables were really good, especially when FDA and other regulators were present. Also great to hear what other companies are doing."
- Associate Director, Bayer Healthcare

"Both conferences were extremely useful. The gamut of important topics were covered, the quality and diversity of presentations was outstanding."
- Senior Scientist, Pfizer

"It was a great conference and I enjoyed all the talks; Good content and good networking opportunities.
Nice mix of US and EU speakers."
- Principal Scientist and Director, Genentech

"This event addressed the most important questions in the field."
- Chemist, Lab of Plasma Proteins, FDA

SPONSORSHIP OPPORTUNITIES

Cambridge Healthtech Institute (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 earlier will allow you to maximize exposure to hard-to-reach 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 preregistration 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 or plated dinner, plated dinner with specific conversation focus).

Inquire about booth space, branding and more!

Lead Sponsoring Publications:

nature | Science AAAS | The Scientist – Magazine of the Life Sciences

Sponsoring Publications:

BioPharm International | future medicine | Insight Pharma Reports – Expert Intelligence for Better Decisions | PharmaVOICE

Web Partners:

www.PharmCast.com – Pharmaceutical Internet | labroots.com – your science network | pharmaphorum – bringing healthcare together

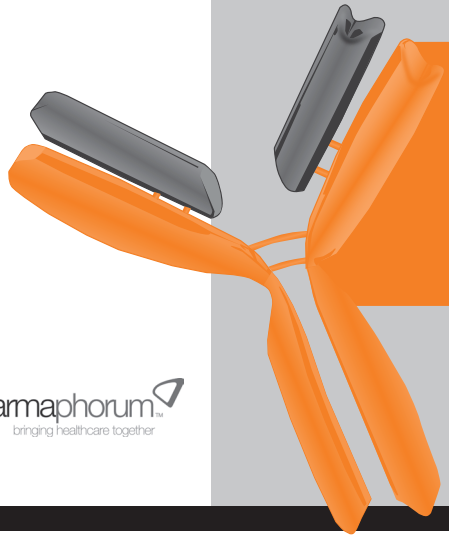
LOOKING FOR ADDITIONAL WAYS TO DRIVE LEADS TO YOUR SALES TEAM?

Cambridge Healthtech Institute can help with custom lead generation programs!

We offer clients numerous options for custom lead generation programs to address their marketing and sales needs. Some of our programs include: live webinars, whitepapers, market surveys, podcasts, and more!

Benefits of working with Cambridge Healthtech Institute for your lead generation needs:

- Your campaign will receive targeted promotion to Cambridge Healthtech Institute's unparalleled database of over 800,000 individuals, representing all sectors of the life sciences – lists can be segmented based on geography, research area, title and industry.
- All custom lead generation programs are promoted through our experienced marketing team that will develop and drive targeted campaigns to drive awareness and leads to your lead generation program.
- For our webinar programs, we offer assistance in procuring speakers for your web symposia through our extensive roster of industry recognized speakers across multiple disciplines within life sciences, as well as provide an experienced moderator and dedicated operations team who will coordinate all efforts.
- If choosing a whitepaper program, we can offer editorial experience and provide an industry recognized author to write your whitepaper.



To customize your participation at this event, contact:
Tim McLucas
Manager, Business Development
781-972-1342
tmclucas@healthtech.com

Pricing and Registration Information

SHORT COURSES

	Commercial	Academic, Government, Hospital-affiliated
One short course	$695	$395
Two short courses	$995	$695
Three short courses	$1295	$895

October 9
SC1: Assays for Measuring Binding Antibodies
SC2: Neutralizing Antibody Assays
SC3: Navigating the Regulatory Hierarchy of Concerns to Minimize Impact of Immunogenicity-Related Risks on Product Registration *(Dinner Short Course)*

SUMMIT PRICING - BEST VALUE!

(Includes access to both conferences, excludes short courses)

Advance registration discount until September 14, 2012	$2575	$1075
Registration after September 14, 2012 and on-site	$2725	$1145

SINGLE CONFERENCE PRICING

(Includes access to one conference, excludes short courses)

Advance registration discount until September 14, 2012	$1655	$825
Registration after September 14, 2012 and on-site	$1865	$945

October 10-11	October 11-12
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 September 12, 2012. 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 registration form 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

If you are unable to attend but would like to purchase the Immunogenicity Summit 2012 CD for $350 (plus shipping), please visit ImmunogenicitySummit.com. Massachusetts delivery will include sales tax.

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.

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!

Cambridge Healthtech Institute
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