10th Annual

# Immunogenicity & Bioassay Summit

Technologies and Strategies for Safe and Efficacious Products in the Clinic

**The Westin Alexandria | Washington, DC** **October 22–25, 2018**

## Conferences:

- Immunogenicity Assessment & Clinical Relevance
- Immunogenicity Prediction & Control
- Optimizing Bioassays for Biologics
- Symposium: Immunology for Biotherapeutics
  Monday October 22

## Training Seminar:

Introduction to Design of Experiments (DoE)

## Plus!

**6** Short Courses, exhibits, posters, and more.

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"This event has a great atmosphere for networking and learning about new expectations in our always changing field."
***- Senior Group Leader, Immunogenicity, PPD, Inc.***

## Keynote Speakers:

**Theresa J. Goletz, PhD**
*Global Head, New Biological Entities and Drug Disposition, EMD Serono Research & Development Institute, Inc.*

**Timothy Hickling, PhD**
*Immunogenicity Sciences Lead, Biomedicine Design, Pfizer, Inc.*

**Thomas Little, PhD**
*President and CEO, Bioassay Sciences, Thomas A. Little Consulting*

**Timothy Schofield**
*Senior Advisor, Technical Research & Development, GSK*

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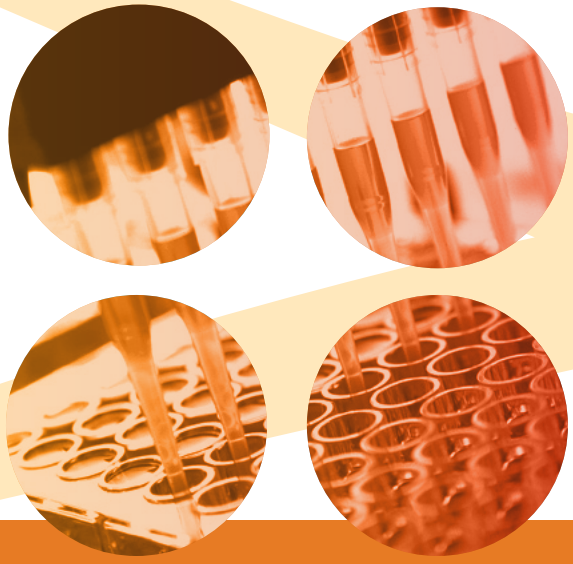
Organized by Cambridge Healthtech Institute

**ImmunogenicitySummit.com**

# Celebrating 10 Years of Progress

Now in its 10th year, CHI's Immunogenicity & Bioassay Summit will examine the challenges currently facing the industry and will provide NEW case studies, NEW perspectives and NEW approaches. You will hear from the industry, academia and the regulatory authorities. This year we present 3 Conferences, a Symposium, Training Seminar and many short courses for in-depth study, as well as interactive breakout discussions for sharing of experiences and ideas, and excellent networking opportunities.



## Conference At-a-Glance

### Monday | October 22

Symposium*: Immunology for Biotherapeutics

**Sc**

**SC1:** Developing Neutralizing Antibody (Nab) Assays

**Sc**

**SC2:** Overcoming Drug Target Interference in ADA Assays

**Sc**

**Dinner SC3:** Validation of ADA Assays and Cut Point Calculations

**Dinner SC4:** Immunology for Immuno-Oncology

### Tuesday | October 23

**C1:** Immunogenicity Assessment & Clinical Relevance

Training SEMINARS By Cambridge Healthtech Institute

**Training Seminar*: TS1:** Intro to DoE

**Reception**

### Wednesday | October 24

**C1:** Immunogenicity Assessment & Clinical Relevance

Training SEMINARS By Cambridge Healthtech Institute

**Training Seminar*: TS1:** Intro to DoE

**C2:** Immunogenicity Prediction & Control

**C3:** Optimizing Bioassays for Biologics

**Sc**

**Dinner SC6:** Advice on Putting Together an Integrated Summary of Immunogenicity

**Sc**

**Dinner SC5:** Back to Basics: Optimizing Bioassay Design and Analysis

### Thursday | October 25

**C2:** Immunogenicity Prediction & Control

**C3:** Optimizing Bioassays for Biologics

*See Registration Page for pricing details.*

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#IMN18

# Sponsorship, Exhibit, and Lead Generation Opportunities



Comprehensive 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.

## PODIUM PRESENTATIONS — *Available within Main Agenda!*

Showcase your solutions to a guaranteed, targeted audience through a 15- or 30-minute presentation during a specific conference program, breakfast, lunch, or separate from the main agenda within a pre-conference workshop. Package includes exhibit space, on-site branding, and access to cooperative marketing efforts by CHI. For the luncheon option, lunches are delivered to attendees who are already seated in the main session room. Presentations will sell out quickly, so sign on early to secure your talk!

## ONE-ON-ONE MEETINGS

Select your top prospects from the pre-conference registration list. CHI will reach out to your prospects and arrange the meeting for you. A minimum number of meetings will be guaranteed, depending on your marketing objectives and needs. A very limited number of these packages will be sold.

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

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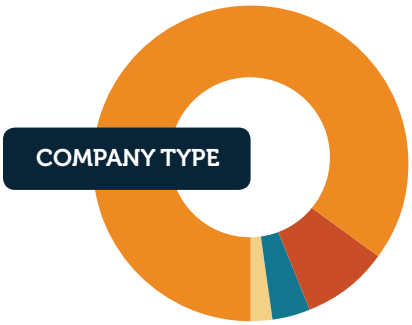
For additional information regarding sponsorship and exhibit opportunities, please contact:

**Carolyn Benton**
*Business Development Manager*
781-972-5412 | cbenton@healthtech.com

# 2017 SUMMIT STATS

## COMPANY TYPE



| | |
|---|---|
| Biotech + Pharma | 85% |
| Academic & Government | 9% |
| Healthcare | 4% |
| Other (Financial, Press, Services) | 2% |

## LOCATION

| | |
|---|---|
| USA | 81% |
| Europe | 10% |
| Asia | 5% |
| Rest of World | 4% |

**US BREAKDOWN**

| | |
|---|---|
| East Coast | 66% |
| West Coast | 20% |
| Midwest | 14% |

## DELEGATE TITLE

| | |
|---|---|
| Scientist/Technologist | 39% |
| Executive + Director | 31% |
| Manager | 14% |
| Sales & Marketing | 10% |
| Professor | 3% |
| Other | 3% |

250+ Delegates

FROM 145 Companies

60 Speakers

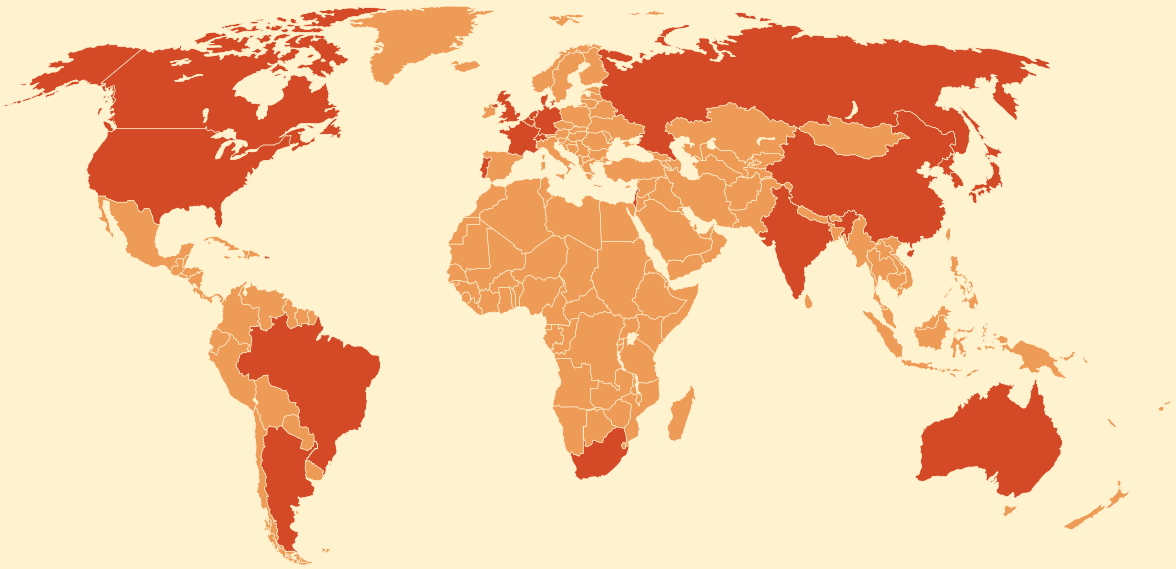
25 POSTERS

14 Exhibiting Companies

> *I think your conference is one of the best ones focused on immunogenicity. Your ability to attract multiple FDA speakers is a big plus.*
> ***–CSO, Selecta Biosciences***

> *Always an excellent meeting for measuring the pulse of the industry and gaining insight about trends and challenges from thought leaders and regulators alike.*
> ***–Research Scientist, Immunology, Charles River Labs Preclinical Services, Montreal Inc.***

## 15 Countries Represented



# Distinguished Faculty

*Mitra Azadeh, PhD,* Principal Scientist, Bioanalytical & Biomarker Development, Nonclinical Development, R&D, Shire

*Robyn Beckwith, PhD,* Technical Development Scientist, Analytical Development and Quality Control, Genentech

*Steve Bowen, PhD,* Team Leader, Chemist, Office of Biotechnology Products, CDER, FDA

*Keith M. Bower,* Principal CMC Statistician, Process Sciences, Seattle Genetics

*Sivan Cohen, PhD,* Scientist, BioAnalytical Sciences, Genentech, Inc.

*Terry P. Combs, PhD,* Senior Scientist, BioMedicine Design, Pfizer, Inc.

*Rakesh Dixit, PhD,* Vice President, R&D, Global Head, Biologics Safety Assessment, MedImmune, Inc.

*Mark Fogg, PhD,* Head, Immunology, Biology, Abzena

*Jochem Gokemeijer, PhD,* Associate Director, Molecular Discovery Technology, Bristol-Myers Squibb

*Theresa J. Goletz, PhD,* Global Head, New Biological Entities and Drug Disposition, EMD Serono Research & Development Institute, Inc.

*William Hallett, PhD,* Biologist, OPQ/OBP, CDER, FDA

*Stephen Hartman, PhD,* Senior Scientist III, AbbVie

*Timothy Hickling, PhD,* Immunogenicity Sciences Lead, Biomedicine Design, Pfizer, Inc.

*Sylvia Janetzki, MD,* President, ZellNet Consulting

*Samantha Jeshonek, PhD,* Research Informatics Analyst, Research Informatics, Collaborative Drug Discovery

*Zhihua Jiang, PhD,* Senior Scientist, BioMedicine Design, Pfizer, Inc.

*Martin Kane, MS, CRE,* Managing Data Scientist, Statistical and Data Sciences Practice, Exponent

*Indigo King, PhD,* Scientist, Immunology, Cyrus Biotechnology

*Kei Kishimoto, PhD,* CSO, Selecta Biosciences

*Michael Lacy, PhD,* Lead Scientist, Non-Clinical Development, Emergent BioSolutions

*David Lansky, PhD,* President, Precision Bioassay, Inc.

*Kevin Larimore, PhD,* Senior Scientist, Bioanalytical Sciences, BioMarin Pharmaceutical, Inc.

*Karen Liao, MD,* Investigator, GSK Associate Fellow, Immunogenicity and Clinical Immunology, GlaxoSmithKline

*Thomas Little, PhD,* President and CEO, Bioassay Sciences, Thomas A. Little Consulting

*Jad Maamary, PhD,* Senior Scientist, Merck and Co., Inc.

*Lilia Macovei, PhD,* Senior Scientist, BioMedicine Design, Pfizer, Inc.

*Mauricio Maia, PhD,* Senior Scientist, BioAnalytical Sciences, Genentech, Inc.

*David H. Margulies, MD, PhD,* Chief, Molecular Biology, Immunology Lab, NIAID, National Institutes of Health

*Ronit Mazor, PhD,* Scientist, Antibody Discovery & Protein Engineering (ADPE), MedImmune, Inc.

*Jim McNally, PhD,* Senior Director, Therapeutic Area Lead, Non-Clinical Development, Shire

*Devangi Mehta, PhD,* Associate Director, Development Biomarkers and Bioanalytical Sciences, Biogen, Inc.

*J. Joseph (Jos) Melenhorst, PhD,* Director, Product Development & Correlative Sciences, Cellular Immunotherapies, University of Pennsylvania

*Paul Moore, PhD,* Vice President, Immunology and Cell Biology, Macrogenics, Inc.

*Steven Novick, PhD,* Director, Statistical Sciences, MedImmune

*Michael Partridge, PhD,* Senior Staff Scientist, Bioanalytical Sciences, Regeneron Pharmaceuticals, Inc.

*Sofie Pattijn,* CTO, ImmunXperts

*Joao Pedras-Vasconcelos, PhD,* Biotech Quality and Immunogenicity Reviewer, Office of Biotechnology Products, CDER, FDA

*Brian R. Peterson, PhD,* President, Bioassay Solutions LLC

*Valerie Quarmby, PhD,* Staff Scientist, BioAnalytical Sciences, Genentech, Inc.

*Bonita (Bonnie) Rup, PhD,* Biopharmaceutical Consultant, Bonnie Rup Consulting

*Christian Ruzanski, PhD,* Senior Scientist, Bioanalysis, Novo Nordisk A/S

*Zuben E. Sauna, PhD,* Principal Investigator, Plasma Protein Therapeutics, CBER, FDA

*Timothy Schofield,* Senior Advisor, Technical Research & Development, GSK

*Mingfang Shen,* Principal Development Associate, Translational Research, ImmunoGen, Inc.

*Ethan Shevach, MD,* Senior Investigator, Laboratory of Immunology, National Institute of Allergy and Infectious Diseases, NIH

*Han-Yu Shih, PhD, MS,* Research Fellow, National Institute of Arthritis and Musculoskeletal and Skin Disease, (NIAMS), NIH

*Renu Singh-Dhanikula, PhD,* Senior Research Investigator, Metabolism & Pharmacokinetics, Bristol-Myers Squibb

*Noel Smith, PhD,* Senior Group Leader, Applied Protein Services, Lonza Pharma & Biotech

*Perceval Sondag,* Senior Manager, Statistics, PharmaLex

*Chris Stebbins, PhD,* Principal Scientist, Translational Medicine, Biogen, Inc.

*Lauren Stevenson, PhD,* Director, Development Biomarkers and Bioanalytical Sciences, Biogen, Inc.

*Daniela Verthelyi, PhD,* Chief, Immunology Lab, Therapeutic Proteins, FDA, CDER

*Joleen T. White, PhD,* Director, Head of Project Support, NBE Drug Disposition, EMD Serono

*Annemie Wielant,* Senior Scientist, Bioassay Development, UCB

*Weifeng Xu, PhD,* Senior Research Investigator, Bioanalytical Science, Bristol-Myers Squibb

*Li Xue, PhD,* Senior Principal Scientist, BioMedicine Design, Pfizer, Inc.

*Haoheng Yan, PhD, MD,* Chemist, OPQ/OBP, CDER, FDA

# Symposium: Immunology for Biotherapeutics* October 22, 2018

## Understanding and Manipulating the Immune System for Therapeutic Advantage

*See Registration Page for pricing details.

Many of the exciting developments in drug discovery and development today concern the immune response and its manipulation and control. Our understanding of immune involvement in therapeutic disorders and their treatment is developing rapidly. T and B lymphocyte subsets, innate lymphoid cells (ILCs), macrophages, dendritic cells and cytokines are all involved in a complex manner. There is the potential for manipulation for therapeutic advantage, yet the danger of disastrous consequences if not well understood. At this symposium, attendees will find out how to utilize the immune system and overcome inhibitory factors without overlooking potential safety issues.

## MONDAY, OCTOBER 22

**8:30 am Registration and Morning Coffee**

**9:30 Chairperson's Opening Remarks**

*Ethan Shevach, MD, Senior Investigator, Laboratory of Immunology, National Institute of Allergy and Infectious Diseases, NIH*

**9:40 KEYNOTE PRESENTATION: Current Understanding of the Role of T Regulatory Cells and Their Modulation**

*Ethan Shevach, MD, Senior Investigator, Laboratory of Immunology, National Institute of Allergy and Infectious Diseases, NIH*

The major role of the immune system is to provide protective responses to pathogenic microorganisms. The immune system consists of several distinct cell types and each type plays a unique role. Dysregulation of the immune system can result in responses against self-antigens and in the development of autoimmune diseases. A specialized subset of T lymphocytes, termed T regulatory (Treg) cells, functions to suppress anti-self responses. Modulation of Treg function with drugs or biologics represents a major approach to the treatment of autoimmune disease.

**10:15 Antigen Processing and Presentation: The Basis of T-Cell Activation**

*David H. Margulies, MD, PhD, Chief, Molecular Biology, Immunology Lab, NIAID, National Institutes of Health*

Antigen presenting cells process protein antigens into peptides for binding by either Major Histocompatibility Class I (MHC-I) or Class II (MHC-II) molecules, which are then displayed at the cell surface as peptide/MHC complexes where they are recognized by T-cell receptors leading to T-cell activation. Cell biological, biochemical, and structural details of these processes as we now understand them will be discussed.

**11:00 Networking Coffee Break**

**11:30 Current Understanding of the Role of the Innate Immune System and Implications for Biotherapeutics**

*Han-Yu Shih, PhD, MS, Research Fellow, National Institute of Arthritis and Musculoskeletal and Skin Disease, (NIAMS), NIH*

The field of innate lymphoid cell (ILC) biology has progressed rapidly, with appreciation of these cells' role in immunity, barrier tissue integrity and homeostasis. ILCs can be classified based on their cytokine production profiles that mirror to the patterns in their adaptive CD4 T helper (Th) cell analogs. Unlike Th cells, ILCs respond to pathogens promptly without the need of antigen-specific receptor recognition. Understanding how ILCs differentiate and contribute to the immunoregulation in health and diseases is fundamentally important for development of new strategies to treat autoimmunity, infection and cancer.

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

**12:45 Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

**2:00 Applying Bispecific Technology to Modulate the Immune Response for Therapeutic Intervention**

*Paul Moore, PhD, Vice President, Immunology and Cell Biology, Macrogenics, Inc.*

Bispecific antibody-based molecules afford therapeutic opportunities not feasible with single-target antibodies or combinations. The most advanced clinical strategy in oncology exploits the ability of bispecific molecules to co-engage T-cells with tumor cells resulting in tumor cell lysis and T-cell expansion. Additional approaches to leverage immune cells through bispecific targeting are being explored in oncology, autoimmunity and infectious diseases. These approaches will be summarized in the context of molecule design and target selection.

**2:45 FEATURED PRESENTATION: Immunology Safety Considerations for Biotherapeutics**

*Rakesh Dixit, PhD, Vice President, R&D, Global Head, Biologics Safety Assessment, MedImmune, Inc.*

In this presentation, I shall examine the challenges of biotherapeutics impacting on the immune response, and the challenges investigators face managing, dose, scheduling, and satisfying the regulatory requirements. The checkpoint inhibitors used for immunotherapy have a natural role in controlling autoimmune diseases such as Type 1 Diabetes and Lupus. Immunotherapies in general, and technologies modifying T-cell function and those involving cytokines present dangers of autoimmune disease, cardiovascular disorders, and additional challenges, especially when used in combination.

**3:30 Networking Refreshment Break**

**3:45 Biopharmaceutical Product Immunogenicity: What Causes It and What Are the Safety and Efficacy Consequences?**

*Bonita (Bonnie) Rup, PhD, Biopharmaceutical Consultant, Bonnie Rup Consulting*

Biopharmaceuticals represent a rapidly growing class of therapeutic product, contributing significantly to advancing treatment of serious diseases including chronic inflammatory and autoimmune diseases, genetic deficiencies, and cancer. Unfortunately, unwanted immunogenic responses against some of these products can occur, often reducing efficacy and sometimes causing safety consequences such as hypersensitivity, immune complex disease, and autoimmune syndromes. In this talk, factors that affect the degree to which the immune system responds, and the degree to which the response affects the efficacy and safety are discussed.

**4:30 Vaccines: Understanding the Mode of Action, Progress to Date, and Ongoing Challenges**

*Michael Lacy, PhD, Lead Scientist, Non-Clinical Development, Emergent BioSolutions*

Complex immune responses result from the complexity of whole pathogen vaccines. Vaccines can be simplified to 3 general components, each of which is supplied by whole pathogens in a convenient package. Despite complex immunity within the recipient, measurements are limited usually to net immunity assessments. Emerging safety issues may lead to purified and quantified vaccine components. Purified immune stimulants that mimic native stimulants may be effective. Formulations may preserve epitopes and control unwanted immunity. Selection of conserved epitopes may bypass rapid mutational rates of pathogens.

**5:15 Discussion**

**5:30 Close of Symposium**

**5:30 Dinner Short Course Registration**

**6:15-9:15 Recommended Dinner Short Course***

**SC4: Immunology for Immuno-Oncology**

** Separate registration required, see page 7 for details.*

# Short Courses*

Enrich Your Conference Experience

October 22 & 24, 2018

*See Registration Page for pricing details.

## MONDAY, OCTOBER 22

### MORNING | 10:00 AM - 1:00 PM

### SC1: Mechanism of Action and Risk-Based Approach for Developing Neutralizing Ab Assays

*Instructors: Jim McNally, PhD, Senior Director, Therapeutic Area Lead, Non-Clinical Development, Shire*

*Weifeng Xu, PhD, Senior Research Investigator, Bioanalytical Science, Bristol-Myers Squibb*

The development of neutralizing antibody assays is a daunting task that is complicated by the specific nature of each biotherapeutic. Many factors must be assessed to choose the proper assay format, to develop a robust assay and for working out when to invest in the development and implementation of these assays. This short course will focus on these topics and provide examples of current industry practices and publications. Specific focus will be given to a mechanism of action-based approach to selecting the assay format. Relevant case studies will be provided.

Topics covered include:

- Current regulatory guidance
- NAb assay strategy – Immunogenicity risk assessment
- Assay format selection – Mechanism of action based approach
- Validation and implementation of NAb assays
- Case studies

### AFTERNOON | 2:30 - 5:30 PM

### SC2: Overcoming Drug Target Interference in ADA Assays

*Instructors: Jim McNally, PhD, Senior Director, Therapeutic Area Lead, Non-Clinical Development, Shire*

*Lilia Macovei, PhD, Senior Scientist, BioMedicine Design, Pfizer, Inc.*

Soluble drug or drug target can often interfere in the detection of anti-drug antibodies. Although not always straightforward, it can be addressed and mitigated in a properly designed immunoassay. This short course will give an overview of the different types of interferences and current methodologies and approaches being utilized to resolve or reduce them.

Topics covered include:

- Types of interferences
- Immunogenicity assay designs and susceptibility to interference
- Mitigation strategies
- Case studies

### DINNER SHORT COURSES | 6:15 - 9:15 PM

### SC3: Validation of ADA Assays and Cut Point Calculations

*Instructors: Jim McNally, PhD, Senior Director, Therapeutic Area Lead, Non-Clinical Development, Shire*

*Michael Partridge, PhD, Senior Staff Scientist, Bioanalytical Sciences, Regeneron Pharmaceuticals, Inc.*

This short course will focus on the validation of ADA Assays and Cut Point evaluations. We will provide an in-depth overview of the basic considerations around ADA assay validation, with significant focus on the process of evaluating different types of cut points, and the translation of the cut point established during validation to the real-world implementation during a preclinical or clinical study.

Topics covered include:

- Tiered Testing Strategy – Basic issues regarding screening, confirmatory and titer assays
- ADA Assay Validation Strategies – Experimental design to execute a validation
- Stepwise process for calculating different types of cut points
- Practical challenges for the in-study implementation of cut points
- Case studies related to the implementation of validation and study specific cut points

### SC4: Immunology for Immuno-Oncology

#### Part One: Harnessing the Body's Natural Immune Response to Fight Cancer

*Instructor: Jochem Gokemeijer, PhD, Associate Director, Molecular Discovery Technology, Bristol-Myers Squibb*

Checkpoint inhibitors as a cancer treatment have shown remarkable response rates in previously hard-to-treat cancers by redirecting the body's own immune system to recognize and eliminate tumor cells. Here we will discuss the current state of immune-oncology agents in the clinic, challenges related to toxicities, biomarker approaches for patient stratification, and future directions of the field.

#### SC4: Part Two: Adoptive T Cell Therapy

*Instructor:J. Joseph (Jos) Melenhorst, PhD, Director, Product Development & Correlative Sciences, Cellular Immunotherapies, University of Pennsylvania*

The early realization that cancer patients may exhibit tumor-resident or circulating T cells that respond to the tumor has led to a flood of basic and translational studies aimed at characterizing the antigens recognized by T cells and the T cell receptor (TCR) chains responsible for this tumor specificity. Biotechnological developments, fueled by discoveries in basic immunology, have led to the introduction of man-made tumor-targeting receptors made up of B cell and T cell domains, currently known as chimeric antigen receptors or CARs. In my talk, I will discuss the evolving field of adoptive T cell therapy, and compare and contrast tumor targeting efforts with allogeneic, autologous minimally manipulated to the TCR and CAR-redirected T cells. Topics to discuss are safety, efficacy, toxicity, clinical trials in hematologic and solid tumors, and future directions to enhance immunogene therapy of cancer.

## WEDNESDAY, OCTOBER 24

### DINNER SHORT COURSES | 6:15 - 9:15 PM

### SC5: Back to Basics: Optimizing Bioassay Design and Analysis

*Instructors: Sofie Pattijn, CTO, ImmunXperts*

*Annemie Wielant, Senior Scientist, Bioassay Development, UCB*

*Sylvia Janetzki, MD, President, ZellNet Consulting*

Bioassays are used broadly and frequently in today's labs to determine the potency of biopharmaceuticals by testing their effects on living cells. With the main focus commonly being set on obtainable results and data handling, the fundamentals of properly choosing and setting up bioassays are less frequently addressed. This course focuses on the basic questions and challenges of setting up and running bioassays. From the initial scientific question that needs to be answered with the right assay and sample choice to basic set-up strategies that will ultimately determine the assay performance and outcome, an overview will be given of important sample handling considerations, reagent choices, critical protocol steps and available harmonization guidelines. Challenges and pitfalls during the design of a bioassay will also be reviewed and examples of case studies will be presented.

Topics covered include:

- Assay choice
- Sample choice and sample handling considerations
- Critical reagent choices
- Available guidance for essential protocol steps
- Lab examples of bioassay design and set-up

### SC6: Advice on Putting Together an Integrated Summary of Immunogenicity

*Instructors: Joao Pedras-Vasconcelos, PhD, Biotech Quality and Immunogenicity Reviewer, Office of Biotechnology Products, CDER, FDA*

*Bonnie Rup, PhD, Bonnie Rup Consulting LLC*

The purpose of this workshop is to share experience gained in preparing and reviewing the "Integrated Summary of Immunogenicity", with case examples to illustrate the multi-disciplinary information that is most useful for the regulator assessing the scale of risk of undesirable immunogenicity for overall clinical benefit vs. risk. It will examine the sponsor team's role and provide examples of how to address potential issues (and avoid introducing any new ones!) by generating a well-thought-out and constructed integrated summary.

Topics covered include:

- Defining the gap: Priorities for the regulator; common gaps in dossiers; examples of Agency questions triggered by missing information; the regulator's recommendations
- Addressing the gap: Suggested structure; relationship to other parts of the dossier; what, where and how? Examples to illustrate how to present relevant information.
- The role of the sponsor team
- Interactive discussion: Using the Integrated Summary of Immunogenicity to minimize regulatory questions at the marketing authorization stage

# C1: Immunogenicity Assessment & Clinical Relevance

## Assay Strategy for Meaningful Evaluation

The industry continues to be challenged by the development, application and interpretation of immunogenicity assays. Recently, the FDA has advocated a more stringent approach for cut point setting and assay validation, creating further difficulties. Moreover, the industry remains uncertain about when the more challenging neutralizing antibody assays should be applied, and which type of assay is reliable and acceptable. Additional ongoing challenges concern managing drug and target interference, understanding and handling the impact of pre-existing antibodies, and interpreting the clinical significance of assay data.

**Recommended Pre-Conference Short Courses***

- October 22, 10:00 am – 1:00 pm: SC1: Mechanism of Action and Risk-Based Approach for Developing Neutralizing Ab Assays
- October 22, 2:30 – 5:30 pm: SC2: Overcoming Drug Target Interference in ADA Assays
- October 22, 6:15 – 9:15 pm: SC3: Validation of ADA Assays and Cut Point Calculations

**Recommended Pre-Conference Symposium***

- October 22: Immunology for Biotherapeutics

** Separate registration required, see pages 6-7 for details.*

## TUESDAY, OCTOBER 23

**7:30 am Registration and Morning Coffee**

### CRITICAL ISSUES IN CUT POINTS AND ADA ASSAY VALIDATION

**8:25 Chairperson's Opening Remarks**

*Lauren Stevenson, PhD, Director, Development Biomarkers and Bioanalytical Sciences, Biogen, Inc.*

**8:30 Case Study on Delineation of Immunogenicity Confirmatory Assay Full Validation Strategy, and Implementation of Assay Cut Point Factor Assessment Guidelines**

*Mauricio Maia, PhD, Senior Scientist, BioAnalytical Sciences, Genentech, Inc.*

This presentation will delineate the approach we are following for full-validation of confirmatory immunogenicity assays. We will also outline the strategy currently in place at Genentech for scientifically sound implementation of clinical assay in-study cut points (CPs). Our new practices provide improved clarity and efficient decision-making for when and how CPs should be reset. With multiple specific recommendations, our strategy also allows for careful consideration of each project's unique context, including its immunogenicity risk-assessment.

**9:00 *In vitro* Immunogenicity Assay Analytical Validation and Harmonization**

*Jochem Gokemeijer, PhD, Associate Director, Molecular Discovery Technology, Bristol-Myers Squibb*

Immunogenicity assays are widely used preclinically in biologics drug development to assess immunogenicity liabilities and select development candidates. Variations in assay set ups, lack of common standard, or agreed upon analytical validation make it challenging to compare results and limit the utility of these assays. Here we will discuss analytical validation as well as cross-industry work to harmonize these assays.

**9:30 Reporting Clinically Relevant ADA Data: The Importance of Determining Appropriate Cut Points & Critical Reagents**

*Michael Partridge, PhD, Senior Staff Scientist, Bioanalytical Sciences, Regeneron Pharmaceuticals, Inc.*

Selection of ADA assay cut points is critical as it determines the threshold for positivity. Furthermore, numerous assay-related factors impact method performance and the data generated. ADA cut points are greatly affected by the population (normal/diseased) selected to determine these values, the number of samples, and the statistical approach for outlier removal. Storage conditions for critical reagents can also impact ADA results, increasing false positives and unnecessary confirmation analysis. Cases studies will be presented discussing the impact of these factors on immunogenicity assessment for biotherapeutics.

**10:00 Sponsored Presentation** *(Opportunity Available)*

**10:15 Coffee Break in the Exhibit Hall with Poster Viewing**

### MANAGING INTERFERENCE IN ADA AND NAB ASSAYS

**10:55 Understanding and Overcoming Drug Interference in NAb Bioassays**

*Zhihua Jiang, PhD, Senior Scientist, BioMedicine Design, Pfizer, Inc.*

Neutralizing antibodies (NAb) bioassay relevant to drug mode of action is recommended by the regulatory authorities for immunogenicity assessment. However, drug interference is a significant obstacle in NAb bioassay development comparing to ADA assay. This talk will present a few case studies, in which different strategies were developed for sample pre-treatment to improve drug tolerance of bioassay. The analytical challenges in overcoming drug interference of NAb bioassay will be discussed.

**11:25 ADA Interference of PK Immunoassays in Preclinical Studies**

*Christian Ruzanski, PhD, Senior Scientist, Bioanalysis, Novo Nordisk A/S*

An important prerequisite in understanding the PK, PD, and their relationship to safety of a therapeutic is the accurate measurement of the therapeutic's concentration in non-clinical and clinical samples. ADAs can interfere with the concentration measurement of therapeutic levels and accordingly prevent accurate details about *in vivo* exposure. Here we present two case studies of homogenous PK immunoassays in the non-clinic where ADA assay inference prevented accurate concentration determination of the therapeutic in the highest dose group.

**11:55 Alternatives to the Current Acid-Dissociation-Based Anti-Drug Antibody Extraction to Increase ADA Recovery in Immunogenicity Testing**

*Weifeng Xu, PhD, Senior Research Investigator, Bioanalytical Science, Bristol-Myers Squibb*

Drug-interference is a big challenge for immunogenicity testing for monoclonal Ab therapeutics. Although Beads-Extraction with Acid Dissociation (BEAD) has been successfully developed to overcome drug interference, ADAs can be denatured and lost during the process due to harsh acid treatment. An alternative way of overcoming drug interference other than acid-dissociation is much needed to preserve ADA activity. A couple of innovative approaches will be discussed in this presentation.

**12:25 pm Sponsored Presentation** *(Opportunity Available)*

**12:55 Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

**1:25 Session Break**

### CLINICALLY RELEVANT ADA ASSAYS / MANAGING PRE-EXISTING ANTIBODIES

**2:25 Chairperson's Remarks**

*Michael Partridge, PhD, Senior Staff Scientist, Bioanalytical Sciences, Regeneron Pharmaceuticals, Inc.*

**2:30 Developing Robust ADA Assays Focused on Clinically Relevant Responses**

*Chris Stebbins, PhD, Principal Scientist, Translational Medicine, Biogen, Inc.*

Unlike PK assays, ADA assays need appropriate background to be preserved for ideal performance. This presentation will describe the redevelopment of assays to appropriately capture biological variability and ensure detection of a clinically relevant response. Case studies will be presented.

**3:00 KEYNOTE PRESENTATION: Impact of Presence of Pre-Existing Antibodies on Immunogenicity Assessment Strategy**

*Theresa J. Goletz, PhD, Global Head, New Biological Entities and Drug Disposition, EMD Serono Research & Development Institute, Inc.*

While all biotherapeutics have the potential to induce an antidrug antibody response (ADA), for some, pre-existing ADAs are observed in drug-naïve matrix. The presence of pre-existing ADAs may influence the bioanalytical approach and data analysis, both preclinically and clinically. Clinical case studies of biotherapeutic candidates in development for oncology or non-oncology indications for which pre-existing ADA were detected will be presented.

### 3:30 Assay Design Strategies and Clinical Impact of Pre-Existing ADA

*Kevin Larimore, PhD, Senior Scientist, Bioanalytical Sciences, BioMarin Pharmaceutical, Inc.*

Situations where anti-drug antibodies (ADAs) are present in a large fraction of untreated individuals present particular challenges for ADA assay development. We will discuss several non-standard approaches to cut point assessment for anti-PEG antibody assay design that were implemented to overcome the challenge of pre-existing anti-PEG antibodies in clinical trial subjects before initiation of treatment. The clinical impact of pre-existing and treatment-induced anti-PEG antibodies will be discussed.

### 4:00 Refreshment Break in the Exhibit Hall with Poster Viewing

### 4:40 Problem Solving Roundtable Discussions

**Table 1: Cutpoints for Screening and Confirmatory Assays: Managing Change**
*Moderator: Mauricio Maia, PhD, Senior Scientist, BioAnalytical Sciences, Genentech, Inc.*

**Table 2: Dealing with Pre-Existing Positive ADA Activity in Study Patients**
*Moderator: Theresa J. Goletz, PhD, Global Head, New Biological Entities and Drug Disposition, EMD Serono Research & Development Institute, Inc.*

**Table 3: Challenges in Developing Neutralizing Antibody Assays**
*Moderator to be Announced*

**Table 4: The Challenge of Drug- and Matrix-Interference in Immunogenicity Testing**
*Moderator: Weifeng Xu, PhD, Senior Research Investigator, Bioanalytical Science, Bristol-Myers Squibb*

**Table 5: Late Stage Clinical and Post-Marketing Strategies: Evolving ADA Assays Over Time**
*Moderator: Mitra Azadeh, PhD, Principal Scientist, Bioanalytical & Biomarker Development, Shire*

**Table 6: Meeting Regulatory Expectations Regarding Immunogenicity Assessment**
*Moderator to be Announced*

**Table 7: Immunogenicity Testing for Biosimilars**
*Moderator to be Announced*

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

### 6:30 Close of Day

## WEDNESDAY, OCTOBER 24

### 7:30 am Morning Coffee

## THE QUEST FOR CLINICALLY MEANINGFUL NAB ASSAYS / REGULATORY PERSPECTIVES

### 7:55 Chairperson's Remarks

*Theresa J. Goletz, PhD, Global Head, New Biological Entities and Drug Disposition, EMD Serono Research & Development Institute, Inc.*

### 8:00 Case Study on Post-Marketing Requirement to Develop an Appropriately Sensitive NAB Assay: Is It Clinically Meaningful?

*Devangi Mehta, PhD, Associate Director, Development Biomarkers and Bioanalytical Sciences, Biogen, Inc.*

This presentation will highlight lessons learned during the development of low-risk monoclonal antibody therapeutics regarding the incidence and impact of immunogenicity. A case study will be presented that evaluates the cost versus value gained of developing, validating, and deploying neutralizing antibody assays for a low risk molecule versus using the "biomarkers of NAbs" approach.

### 8:30 FEATURED PRESENTATION: Best Practices for Successful Immunogenicity Assay Review by the Agencies

*William Hallett, PhD, Biologist, OPQ/OBP, CDER, FDA*

An immunogenicity assessment often includes validated screening, confirmatory, and neutralizing assays at the time of BLA submission. The submission of validation reports that occasionally include poorly defined criteria and confusing nomenclature leads to information requests that may result in miscommunication between reviewers and sponsors, resulting in delays. This talk will focus on best practices to improve the quality of immunogenicity submissions.

### 9:00 FDA Regulatory Perspective on Immunogenicity Testing for Biosimilars

*Haoheng Yan, PhD, MD, Chemist, OPQ/OBP, CDER, FDA*

A clinical study or studies assessing the immunogenicity of the proposed biosimilar product and that of the innovator product is essential in a 351(k) application (biosimilar pathway). We will discuss the FDA's expectation on the immunogenicity study design, the assay development and validation, and assessment of results specific to biosimilar applications.

### 9:30 Sponsored Presentation *(Opportunity Available)*

### 10:00 Coffee Break in the Exhibit Hall with Poster Viewing

### 10:40 Development of Neutralizing Antibody Assay for Supporting Chimeric Antigen Receptor T-Cell (CAR-T) Therapy: Lessons and Strategies

*Lilia Macovei, PhD, Senior Scientist, BioMedicine Design, Pfizer, Inc.*

Chimeric Antigen Receptor T-cells (CART) is a personalized therapy that uses the patient's own T cells or healthy donor's T-cells, engineered to express artificial T-cell receptors designed to convey MHC-independent target recognition. These therapies have recently shown great promise in treating hematological cancers. The Nab assay development, unique challenges and immunogenicity strategy to detect anti-CART receptor neutralizing antibodies will be presented.

### 11:10 Case Study on Challenges of Immunogenicity Assessment for a Short Peptide Therapeutic

*Mitra Azadeh, PhD, Principal Scientist, Bioanalytical & Biomarker Development, Shire*

There are unique challenges associated with the development of immunogenicity assays for short peptide therapeutics. Their small size reduces their antigenicity and the likelihood of success for positive control generation. Their shorter sequence also renders them less effective capture and detection agents for standard immunoassays. This presentation reviews the case study of a short peptide drug and the strategies used to develop a sensitive and drug tolerant immunogenicity assay.

### 11:40 Immunogenicity Challenges Surrounding Immunogenicity Assessment of Gene Therapy Vectors

*Terry P. Combs, PhD, Senior Scientist, BioMedicine Design, Pfizer, Inc.*

Environmental exposure to adeno-associated viruses (AAVs) could lead to the production of neutralizing antibodies for current gene therapy vectors. Hence, the transformative power of gene therapy on patients' lives is linked to the standardization of diagnostics for preexisting antibodies (Abs). This presentation will summarize lessons learned thus far from method development research at Pfizer on plate-based assays for preexisting Abs to AAV8 and SPARK-9001 currently in trials for Hemophilia B.

### 12:10 pm Close of Immunogenicity Assessment & Clinical Relevance

# C2: Immunogenicity Prediction & Control

## Regulatory Perspectives, Risk Factors, and Management

The impact of immunogenicity on safety and efficacy, and consequent cost to the industry is well understood. Accordingly, investigators are focusing on factors that contribute to immunogenicity as well as a number of different approaches to predict immunogenicity at the drug discovery stage. There are several major problematic areas such as gene therapy products with viral vectors, and recombinant immunotoxins, and efforts are being made to suppress immune responses to these products and to introduce tolerizing and deimmunization approaches.

**Recommended Pre-Conference Short Courses***

- October 22, 10:00 am – 1:00 pm: SC1: Mechanism of Action and Risk-Based Approach for Developing Neutralizing Ab Assays
- October 22, 2:30 – 5:30 pm: SC2: Overcoming Drug Target Interference in ADA Assays
- October 22, 6:15 – 9:15 pm: SC3: Validation of ADA Assays and Cut Point Calculations

**Recommended Pre-Conference Symposium***

- October 22: Immunology for Biotherapeutics

** Separate registration required, see pages 6-7 for details.*

## WEDNESDAY, OCTOBER 24

**1:00 pm Conference Registration**

### RISK ASSESSMENT / FACTORS CONTRIBUTING TO IMMUNOGENICITY

**1:40 Chairperson's Opening Remarks**

*Ronit Mazor, PhD, Scientist, Antibody Discovery & Protein Engineering (ADPE), MedImmune, Inc.*

**1:45 FDA Regulatory Perspectives on Immunogenicity Risk Assessment from Phase I IND to BLA and Beyond**

*Steve Bowen, PhD, Team Leader, Chemist, Office of Biotechnology Products, CDER, FDA*

Many factors can influence immunogenicity risk associated with biotherapeutic products including the patient population, impurity profile, post-translational modification, and homology to endogenous human proteins. A thorough immunogenicity risk assessment early in product development that evolves throughout clinical development, licensure, and post marketing phases can help avoid costly regulatory delays. This presentation will discuss important considerations for immunogenicity risk assessment at various stages of product development.

**2:15 FEATURED PRESENTATION: Case Studies: Updating Immunogenicity Risk Assessment during Study Conduct**

*Joleen T. White, PhD, Director, Head of Project Support, NBE Drug Disposition, EMD Serono*

Immunogenicity risk assessment is a scientific process that evolves as data emerge. This presentation will discuss when and how you revisit a strategy including case studies about updating immunogenicity risk assessment and adding, removing, or amending associated analyses. It includes: changing the cut point in response to in-study validation results, adding characterization assays for specific purposes, modifying an immunogenicity sampling schedule, and including additional statistical analyses based on preliminary findings.

**2:45 Aggregates and Impurities as Immunogenicity Risk Factors: Case Studies**

*Daniela Verthelyi, PhD, Chief, Immunology Lab, Therapeutic Proteins, CDER, FDA*

Product immunogenicity has emerged as one of the critical roadblocks in the development of biologics, complex generics and biosimilars. This talk will focus on the impact of process-related innate immune response modulating impurities and aggregates on the milieu where the products are delivered highlighting the complex interplay of different impurities on product immunogenicity risk.

**3:15 Sponsored Presentation** *(Opportunity Available)*

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

**4:10 Detection of Memory B Activity for Pre-Existing and Treatment-Induced ADA**

*Karen Liao, MD, Investigator, GSK Associate Fellow, Immunogenicity and Clinical Immunology, GlaxoSmithKline*

We applied a B cell ELISPOT method to evaluate memory B cell activity for pre-existing ADA and treatment-induced ADA against a domain antibody and a humanized monoclonal antibody, respectively. This novel application informs and characterizes immune memory activity associated with ADA responses and can provide a valuable tool for immunogenicity prediction for biologics with elevated risk of ADA.

**4:40 Integrated Modelling Approach to Predict Safety and Immunogenicity of Immunomodulatory Biotherapeutics**

*Renu Singh-Dhanikula, PhD, Senior Research Investigator, Metabolism & Pharmacokinetics, Bristol-Myers Squibb*

The presentation will show an integrated approach of using data from various *in vitro* assays as well as *in silico* predictions to assess safety and immunogenicity risk of biotherapeutics in early discovery and development. We will showcase how modelling approach can be used to select candidates with a better safety profile. We will also expand upon challenges in understanding the impact of the disease state and inter-patient variability in the immune response, and progress that has been made in this direction.

**5:10 *In vitro* T-Cell Assay to Predict Immunogenicity of Biotherapeutic Products**

*Sivan Cohen, PhD, Scientist, BioAnalytical Sciences, Genentech, Inc.*

Treatment of patients with biotherapeutic protein products may result in immune responses of varying clinical relevance including development of life-threatening anti-drug antibodies (ADA) that can limit product efficacy or impact its safety. Therefore, predicting the risk for immunogenicity of biotherapeutic products at early stages is a crucial need. This presentation will focus on *in silico* analyses and *in vitro* T-cell assay studies to characterize the immunogenic potential of different biotherapeutic proteins and their correlation to the clinically observed outcome.

**5:40 Close of Day**

**5:40 Dinner Short Course Registration**

**Recommended Dinner Short Course***

**6:15 – 9:15: SC6: Advice on Putting Together an Integrated Summary of Immunogenicity**

** Separate registration required, see page 7 for details.*

## THURSDAY, OCTOBER 25

**7:30 am Morning Coffee**

### APPLICATION OF PREDICTIVE TOOLS

**7:55 Chairperson's Opening Remarks**

*Joleen T. White, PhD, Director, Head of Project Support, NBE Drug Disposition, EMD Serono*

**8:00 Immunogenicity Risk Management**

*Valerie Quarmby, PhD, Staff Scientist, BioAnalytical Sciences, Genentech, Inc.*

Every biotherapeutic has the potential to elicit unwanted immune responses, and these may compromise safety and efficacy. Immunogenicity risk ranking methods and tools are often used during lead selection and optimization to assess the likelihood that a biotherapeutic may be immunogenic. These tools can also be used retrospectively for root cause analysis. This talk will provide an overview of the use of these tools in the context of immunogenicity risk management.

### 8:30 KEYNOTE PRESENTATION: Application of Mechanistic Modelling to Prediction of Immunogenicity

*Timothy Hickling, PhD, Immunogenicity Sciences Lead, Biomedicine Design, Pfizer, Inc.*

This presentation will introduce an immunogenicity consortium that coordinates *in vitro* data to simulate clinical immunogenicity incidence and impact. Data related to product, patients and treatment are integrated into mechanistic models for predicting ADA incidence and impact on PK to allow for proactive decision-making when designing clinic trials. A case study of 8000 patients will be presented, showing an example of how Pfizer applies mechanistic modelling to their clinical development program, including an examination of the role of HLA and immune response genes. Additional retrospective analyses incorporating findings from the ABIRISK consortium will be discussed.

### 9:00 Presentation to be Announced

Sponsored by PROIMMUNE

### 9:30 Problem Solving Roundtable Discussions

**Table 1: Practical Application of Immunogenicity Preclinical Risk Assessment**
*Moderator: Steve Bowen, PhD, Team Leader, Chemist, Office of Biotechnology Products, CDER/FDA*

**Table 2: Current and Emerging Predictive Tools: Selecting Candidates and Predicting Clinical Outcome**
*Moderator: Jad Maamary, PhD, Senior Scientist, Merck and Co., Inc.*

**Table 3: Application of Mechanistic Modelling to Prediction of Immunogenicity**
*Moderator to be Announced*

**Table 4: Risk of Immunogenicity of Product and Process-Related Impurities, and Leachables/Extractables**
*Moderators: Daniela Verthelyi, PhD, Chief, Immunology Lab, Therapeutic Proteins, FDA/CDER*
*Mohanraj Manangeeswaran, PhD, Therapeutic Proteins, FDA/CDER*

**Table 5: Progress towards Inducing Immunological Tolerance to Biotherapeutics**
*Moderator: Ronit Mazor, PhD, Scientist, Antibody Discovery & Protein Engineering (ADPE), MedImmune, Inc.*

### 10:30 Coffee Break in the Exhibit Hall with Poster Viewing

### 11:10 Predicting Immune Responses to Therapeutic Proteins: The Promise of Safer Drugs and Improved Clinical Outcomes?

*Zuben E. Sauna, PhD, Principal Investigator, Plasma Protein Therapeutics, CBER, FDA*

Protein therapeutics have become an essential part of modern medicine. The development of immune responses to protein therapeutics can adversely affect safety and/or efficacy, concerns that are underscored by the discontinuation of development of several drugs due to immunogenicity issues. I will discuss progress in developing technological approaches that are useful for the non-clinical risk assessment of immunogenicity, as well as mitigation strategies such as the de-immunization of protein molecules.

### 11:40 *In silico* and *in vitro* Methodology to Assess the Immunogenicity Risk Associated with Target Mediated Effect in Mono versus Combination Therapies

*Jad Maamary, PhD, Senior Scientist, Merck and Co., Inc.*

A methodology describing best practices when analyzing prediction algorithms, sequence databases and *in vitro* tools for immunogenicity assessment is presented. This methodology examines underlying assumptions in antigen processing, MHC-II binding, TCR cross-reactivity and germline prevalence in its impact on immunogenicity to biotherapeutics. Case study: *in silico*/*in vitro* assessment of immunogenicity to monoclonal antibodies in mono and combination therapy is assessed with the described tools.

### 12:10 pm Clinical Relevance of Immunogenicity Risk Assessment Tools and Application for Product Engineering and Selection

*Li Xue, PhD, Senior Principal Scientist, BioMedicine Design, Pfizer, Inc.*

The immunogenicity risks of therapeutic proteins are evaluated with a variety of *in vitro* tools. These tools are used to assess the key immunological events that contribute to the anti-drug antibody (ADA) induction. The presentation will discuss the clinical relevance of the antigen presentation and T cell risk assessment tools. Case studies will be cited to illustrate the application for product testing.

### 12:40 Managing Unwanted Immune Responses to Antibodies Including Utilisation of MHC-Associated Peptide Proteomics (MAPPs)

Sponsored by ABZENA

*Mark Fogg, PhD, Head, Immunology, Biology, Abzena*

This presentation will present accurate and sensitive ways to assess the potential immunogenicity and development of anti-drug antibodies against proteins and antibodies *ex vivo* by measuring CD4+ T cell responses, methods for managing and reducing potential immunogenicity, and introduce MHC-Associated Peptide Proteomics (MAPPs) to augment data sets to better inform immunogenicity risk.

### 1:10 Luncheon Presentation: Immunogenicity Risk Assessment: Using Preclinical Tools during Lead Selection and Optimization

Sponsored by Lonza Pharma & Biotech

*Noel Smith, PhD, Senior Group Leader, Applied Protein Services, Lonza Pharma & Biotech*

High attrition rates of preclinical candidates are primarily caused by lack of efficacy or safety issues. Immunogenicity leads to problems including dangerous cytokine response and/or generation of anti-drug antibodies that neutralize protein activity and/or alter PK/PD. Lonza has developed a comprehensive set of preclinical safety and immunogenicity risk assessment tools. This presentation will describe how these tools, used early in development, aid selection and optimization of candidates and help reduce the risk of failure.

### 1:40 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

## IMMUNOSUPPRESSION AND TOLERANCE INDUCTION

### 2:20 Chairperson's Remarks

*Li Xue, PhD, Senior Principal Scientist, BioMedicine Design, Pfizer, Inc.*

### 2:25 Mitigation of Immunogenicity to AAV Gene Therapy Vectors with Tolerogenic Nanoparticles Enables Re-Treatment for Systemic Gene Therapy Applications

*Kei Kishimoto, PhD, CSO, Selecta Biosciences*

Gene therapy using adeno-associated virus (AAV) vectors has shown great therapeutic potential. However, neutralizing antibody (NAb) responses to AAV prevent the ability to re-dose patients. Vector re-administration is important for pediatric applications, as transgene expression is likely to wane over time. We have shown that co-administration of vector with tolerogenic particles containing rapamycin can block formation of anti-AAV NAbs in mice and non-human primates to enable productive vector readministration.

### 2:55 Immune Tolerance Induction to Recombinant Immunotoxins

*Ronit Mazor, PhD, Scientist, Antibody Discovery & Protein Engineering (ADPE), MedImmune, Inc.*

Recombinant Immunotoxins (RITs) are a genetically engineered category of ADC that treats cancer. Because they contain a bacterial toxin that kills the cancer cells, RITs are very immunogenic to cancer patients with a normal immune system; 100% of patients made high ADA titers, which prevented retreatment and lowered efficacy. This talk will discuss our recent findings of immune tolerance induction to RIT that allow multiple treatment cycles in naïve and mice with pre-existing antibodies. We used two approaches, using free low dose methotrexate and tolerogenic nanoparticles that contain rapamycin.

### 3:25 Removing T-Cell Epitopes with Computational Protein Design

*Indigo King, PhD, Scientist, Immunology, Cyrus Biotechnology*

Computational protein design has the potential to create a novel class of therapeutics with tunable biophysical properties, but immunogenicity remains a concern. We have combined machine learning with structure-based protein design to identify and redesign T-cell epitopes without disrupting function of the target protein or creating new epitopes. We have verified the method experimentally, removing T-cell epitopes from a gene therapy target, an immunotoxin, and GFP while maintaining folding and function.

### 3:55 Close of Immunogenicity Prediction & Control

# C3: Optimizing Bioassays for Biologics

## Merging Science and Statistical Methods for Successful Biological Assay Development

Bioassays, at their core, spring from a fusion of biological and statistical sciences, and are used to measure activity or function of a compound or group of compounds in samples. As the field evolves, new technologies and software are changing the way scientists view experimental design and data analysis. The health authorities and USP have provided guidance for the design and validation of a bioassay; however, they do not discuss solutions to common problems springing from this revolution in technology. At Cambridge Healthtech Institute's Seventh Annual Optimizing Bioassays for Biologics, leaders working in bioanalytical and bioassay development will come together to provide case studies and best practices for handling the most common issues in biological assay development, validation, transfer, and maintenance. There will also be a focus on lifecycle management and design of experiments methods. In addition, new technologies and bioassay formats will be presented along with recommendations for implementation to ensure a steady drug development pipeline.

**Recommended Pre-Conference Training Seminar***

- October 23-24: TS1: Introduction to Design of Experiments

** Separate registration required, see page 14 for details.*

## WEDNESDAY, OCTOBER 24

### 1:00 pm Conference Registration

### LIFECYCLE MANAGEMENT

### 1:40 Chairperson's Opening Remarks

*Perceval Sondag, Senior Manager, Statistics, PharmaLex*

### 1:45 KEYNOTE PRESENTATION: A Lifecycle Approach to Bioassay Validation

*Timothy Schofield, Senior Advisor, Technical Research & Development, GSK*

A bioassay can be viewed as a manufacturing process, with measurements the product. The customer is a decision-maker, and the "quality attributes" are related to accuracy and precision. The analytical target profile lists the requirements for uses throughout the bioassay lifecycle. This talk will outline the stages and elements of a lifecycle approach to bioassay validation, highlighting the opportunities for ensuring the quality of bioassay measurement.

### 2:15 A Quality Approach to Stage One Bioassay Optimization

*Steven Novick, PhD, Director, Statistical Sciences, MedImmune*

The goal of stage one lifecycle management is to develop a reliable process for commercial manufacturing. It is imperative to develop robust bioassays to measure critical and key quality attributes, such as potency and purity of the drug substance and drug product. This presentation will illustrate modern statistical methods applied to a response-surface design to determine the design space for multiple bioassays simultaneously by optimizing the probability to meet specifications.

### 2:45 Assay Performance Qualification: A Fit for Purpose Approach

*Perceval Sondag, Senior Manager, Statistics, PharmaLex*

Recently, the lifecycle management concept for analytical procedures was introduced. It is strongly related to the Quality by Design concept given in the ICH-Q8 guidance. This contrasts with ICH-Q2 recommendations that only focus on the validation step to evaluate the performance of an analytical procedure. ICH-Q2's well-known check-list approach fails to provide assurance of the quality of future results with respect to the intended use of the procedure. This talk proposes a fit for purpose method for assay validation in a lifecycle paradigm, while maintaining a reasonable compromise between producer and patient risks.

### 3:15 BioAssay Express: Introducing BLAT, an Assay Registration System for Biologics

*Sponsored by*

CDD VAULT Complexity Simplified™

*Samantha Jeshonek, PhD, Research Informatics Analyst, Research Informatics, Collaborative Drug Discovery*

BioAssay Express annotates bioassay protocols using semantic web vocabulary, which makes them accessible to both humans and machines. New data is created using a web-based interface, and legacy text-based data is curated with the support of text mining and machine learning methods. We will describe BioLogics Assay Template (BLAT).

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

### 4:10 CPV Application in Bioassays – Strategies to Maintain Lot to Lot Consistency & Prevent Assay Drift

*Mitra Azadeh, PhD, Principal Scientist, Bioanalytical & Biomarker Development, Nonclinical Development, R&D, Shire*

Continued process verification (CPV) is critical to bioassay life cycle management and essential in ensuring that the product output is within pre-established specifications. CPV components include systems for deviation identification, data collection and analysis, and in-process evaluation of qualification standards, and assay quality controls remain central throughout the process. This talk focuses on the role of quality controls in assay trending and monitoring of calibration drift. Factors critical to the production, qualification, and maintenance of quality controls as well as statistical versus graphical methods for control trending will be presented.

### 4:40 PANEL DISCUSSION: Statistical Approaches to Lifecycle Validation

- Opportunities to optimize each step of the lifecycle approach using statistical methods
- Common pitfalls and challenges in utilizing statistics for bioassay development
- Understanding regulatory guidelines (USP/NIBSC/FDA/etc.)
- Strategies for successful collaboration between statisticians and bioassay scientists

*Moderator: Perceval Sondag, Senior Manager, Statistics, PharmaLex*

*Panelists: Timothy Schofield, Senior Advisor, Technical Research & Development, GSK*

*Steven Novick, PhD, Director, Statistical Sciences, Medimmune*

*Mitra Azadeh, PhD, Principal Scientist, Bioanalytical & Biomarker Development, Nonclinical Development, R&D, Shire*

### 5:40 Dinner Short Course Registration

**Recommended Dinner Short Course***

**6:15 – 9:15: SC5: Back to Basics: Optimizing Bioassay Design and Analysis**

** Separate registration required, see page 7 for details.*

## THURSDAY, OCTOBER 25

### 7:30 am Morning Coffee

### STATISTICAL CONSIDERATIONS IN SIMILARITY

### 7:55 Chairperson's Opening Remarks

*Thomas Little, PhD, President and CEO, Bioassay Sciences, Thomas A. Little Consulting*

### 8:00 Near-Universal Equivalence Bounds for Similarity in Bioassays

*David Lansky, PhD, President, Precision Bioassay, Inc.*

Testing for similarity via equivalence tests is an essential part of modern bioassay analyses. Sensitivity analyses show that scaled shifts in parameters measure non-similarity in ways that are assay-independent. These scaled shifts have lower bias and variance than ratio estimates of parameter-specific non-similarity. Well-chosen equivalence bounds for scaled shifts yield assays with limited bias in potency due to non-similarity. This gives us a way to set equivalence bounds for non-similarity informed by the product specification and analytic target profile.

### 8:30 Analytic Similarity: A Review of the FDA Draft Guidance on Evaluating Analytic Similarity

*Martin Kane, MS, CRE, Managing Data Scientist, Statistical and Data Sciences Practice, Exponent*

Analytics equivalence has historically been handled with a statistical test for differences. As the regulatory environment matures, newer statistical methods are being developed to help ensure that two analytic methods are in fact equivalent, and don't just suffer from a lack of difference. This talk will explore the statistical technique outlined in the draft FDA guidance document and discuss some of the perceived pitfalls associated with it.

**9:00 Sponsored Presentation** *(Opportunity Available)*

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**9:30 Problem Solving Roundtable Discussions**

**Table 6: Use of New Technologies in Bioassay Development**
*Moderator: Robyn Beckwith, PhD, Technical Development Scientist, Analytical Development and Quality Control, Genentech*

**Table 7: Benefits of Optimizing Bioassays with Design of Experiments (DoE)**
*Moderator: Martin Kane, MS, CRE, Managing Data Scientist, Statistical and Data Sciences Practice, Exponent*

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**10:30 Coffee Break in the Exhibit Hall with Poster Viewing**

## BIOASSAY VALIDATION STRATEGIES

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**11:10 FEATURED PRESENTATION: Strategic Bioassay Design, Beginning with the End in Mind**

*Thomas Little, PhD, President and CEO, Bioassay Sciences, Thomas A. Little Consulting*

The presentation covers the design and validation of a bioassay. It demonstrates how plate layout, dose selection, outlier identification and removal, curve weighting, replicate strategy, curve fitting method, systems suitability and validity criteria all impact the invalid and OOS rate of the assay. A design of experiments approach to method robustness is presented. Establishing a design space for a bioassay, designing the validation protocols and acceptance criteria justification are presented.

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**11:40 Assessing Bioassay Validation Acceptance Criteria in Relation to Study Design**

*Keith M. Bower, Principal CMC Statistician, Process Sciences, Seattle Genetics*

Limited guidance is provided in regulatory documents for bioassay validation acceptance criteria (AC). This presentation illustrates (i) the interrelationship between intermediate precision (IP) and the coefficient of determination, and (ii) how to assess the likelihood of meeting proposed AC for a given study design. The use of a statistical performance assessment, relating IP to other AC is illustrated.

**12:10 pm The Rush to Validate Bioassay: The Good, the Bad, and the Ugly**

*Brian R. Peterson, PhD, President, Bioassay Solutions LLC*

In many instances, several bioassays are used in drug discovery and product characterization with one method designated for product release testing. The question remains, when does the release method need to be validated? The goal of validation is to establish that the method is in fact 'fit for purpose.' All too often, fit for purpose is driven by what the assay can do rather than by what is needed to build a production system that has sufficient process capability to avoid OOS. The race to market often brings compromises. A continual improvement approach can help address these challenges.

**12:40 Sponsored Presentation** *(Opportunity Available)*

**1:10 Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

**1:40 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing**

## STRATEGIC AND NOVEL BIOASSAY DEVELOPMENT

**2:20 Chairperson's Remarks**

*Martin Kane, MS, CRE, Managing Data Scientist, Statistical and Data Sciences Practice, Exponent*

**2:25 Strategies for a Successful Bioassay**

*Stephen Hartman, PhD, Senior Scientist III, AbbVie*

Bioassays are a critical component of the development and testing strategy of biologic therapies. They are amongst the most challenging test methods to develop, implement, and maintain. The inherent variability of living cells, combined with complicated multi-step procedures, biologically active reagents, long incubation times, diverse readouts and instruments, and complex data analysis come together to make bioassay development extremely challenging. Furthermore, modern biotherapeutics are ever adopting new formats, modalities, novel mechanisms of action, and sometimes multiple mechanisms of action. As these therapies become more structurally and functionally diverse and complex, so do the bioassays needed to enable their development and release.

**2:55 Straight to Automation! The Benefits of Early Implementation in Bioassay Development and Optimization**

*Robyn Beckwith, PhD, Technical Development Scientist, Analytical Development and Quality Control, Genentech*

Bioanalytical testing environments routinely face constraints due to sample throughput, procedural variability, required hands-on time, cost and repetitive strain on analysts. Automation of discrete assay steps or entire end-to-end workflows can potentially alleviate these issues, but practical implementation can be challenging given the inherent complexity of biological assay systems. Strategies for successful development and application of automation for biological assays will be explored, including fit for purpose approaches to implementing new technologies.

**3:25 Development of a Cell-Based Potency Assay for New Modality of ADC Product**

*Mingfang Shen, Principal Development Associate, Translational Research, ImmunoGen, Inc.*

**3:55 Close of Optimizing Bioassays for Biologics**

# TS1: Introduction to Design of Experiments (DoE)

**October 23 – 24, 2018**

## TUESDAY, OCTOBER 23 AND WEDNESDAY, OCTOBER 24

**Day 1: TUESDAY, 8:30 am - 5:30 pm**

**Day 2: WEDNESDAY, 8:00 am - 12:00 pm**

*Instructor: Perceval Sondag, Senior Manager, Statistics, PharmaLex*

This class is an introduction course to the concept of Design of Experiments. First, trainees will learn, using a simple example, the value of DoE and how it can drastically increase the amount of information provided by each experiment. Then, we'll discuss how to choose the appropriate design for different situations. Trainees will have an overview of the DoE catalog, including the advantage of each type of design (Screening designs, Factorial designs, Response-surface designs, Optimal designs). Finally, attendees will gain an appreciation for the many ways output can be used to better understand and optimize processes.

- What is so special about DoE?
- Plan an experiment
- Find the appropriate design
- Overview of DoE catalog
  - o Screening designs
  - o Factorial designs
  - o Response-surface designs
  - o Optimal designs
  - o Mixture designs
- Experiments are planned. Now what?
  - o Analysis of DoE data
  - o Optimization of one or several responses together

**Who should attend**: Members of bioanalytical R&D, those who work in quality control or CMC for biological products, statisticians and biologists who are new to biological assays, and members of industry regulatory groups that support biological products.

### TRAINING SEMINAR INFORMATION

Each CHI Training Seminar offers 1.5 days of instruction with start and stop times for each day shown above and on the Event-at-a-Glance published in the onsite Program & Event Guide. Training Seminars will include morning and afternoon refreshment breaks, as applicable, and lunch will be provided to all registered attendees on the full day of the class. Each person registered specifically for the training seminar will be provided with a hard copy handbook for the seminar in which they are registered. A limited number of additional handbooks will be available for other delegates who wish to attend the seminar, but after these have been distributed, no additional books will be available. Though CHI encourages track hopping between conference programs, we ask that Training Seminars not be disturbed once they have begun. In the interest of maintaining the highest quality learning environment for Training Seminar attendees, and because Seminars are conducted differently than conference programming, we ask that attendees commit to attending the entire program, and not engage in track hopping, as to not disturb the hands-on style instruction being offered to the other participants.

Visit our website for full details on this training seminar:
**ImmunogenicitySummit.com/Training-Seminars**

## Hotel & Travel

**Conference Hotel:**
**The Westin Alexandria**
400 Courthouse Square
Alexandria, VA 22314
Phone: 703-253-8600

**Discounted Room Rate: $242 s/d**

**Discounted Room Rate Cut-Off Date: September 24, 2018**

**Reservations and Additional Travel Information:**
Go to the travel page of ImmunogenicitySummit.com

# PRESENT A POSTER AND SAVE $50!

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by **September 21, 2018.**

Reasons you should present your research poster at this conference:

- Your poster will be seen by our international delegation, representing leaders from top pharmaceutical, biotech, academic and government institutions
- Receive $50 off your registration
- Your poster abstract will be published in our conference materials

## Media Partners

*Lead Sponsoring Publications*

American Laboratory
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nature
Pharmaceutical Outsourcing
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antibodies-online.com
BioSpace
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SelectScience

# Immunogenicity & Bioassay Summit

The Westin Alexandria • Washington, DC • October 22-25, 2018

## Pricing & Registration Information

### PREMIUM PACKAGE – BEST VALUE!

*(Includes access to all conferences, training seminar, and the symposium. You may conference-hop to conferences occurring on the same dates. Excludes access to short courses.)*

| | Commercial | Academic, Government, Hospital-Affiliated |
|---|---|---|
| Early - Registration Rate until August 3, 2018 | $2,699 | $1,299 |
| Advance - Registration Rate until September 21, 2018 | $2,899 | $1,399 |
| Registration after September 21 and on-site | $3,099 | $1,499 |

### STANDARD PACKAGE *(Includes access to one conference or the training seminar and symposium. Excludes access to short courses.)*

| | | |
|---|---|---|
| Early - Registration Rate until August 3, 2018 | $2,449 | $1,149 |
| Advance - Registration Rate until September 21, 2018 | $2,549 | $1,199 |
| Registration after September 21 and on-site | $2,749 | $1,299 |

### SYMPOSIUM - OCTOBER 22

| | | |
|---|---|---|
| Early - Registration Rate until August 3, 2018 | $949 | $599 |
| Advance - Registration Rate until September 21, 2018 | $999 | $699 |
| Registration after September 21 and on-site | $1,049 | $899 |

### SHORT COURSE PRICING

| | | |
|---|---|---|
| One Short Course | $799 | $499 |
| Two Short Courses | $1,049 | $749 |
| Three Short Courses | $1,399 | $999 |
| Four Short Courses | $1,549 | $1,099 |

| Monday \| October 22 | | Tuesday \| October 23 | | Wednesday \| October 24 | | Thursday \| October 25 | |
|---|---|---|---|---|---|---|---|
| Symposium: Immunology for Biotherapeutics | SC1: Developing Neutralizing Antibody (Nab) Assays | C1: Immunogenicity Assessment & Clinical Relevance | TS1: Intro to DoE | C1: Immunogenicity Assessment & Clinical Relevance | TS1: Intro to DoE | C2: Immunogenicity Prediction & Control | C3: Optimizing Bioassays for Biologics |
| | SC2: Overcoming Drug Target Interference in ADA Assays | | | C2: Immunogenicity Prediction & Control | C3: Optimizing Bioassays for Biologics | | |
| | Dinner SC3: Validation of ADA Assays and Cut Point Calculations | | | Dinner SC5: Back to Basics: Optimizing Bioassay Design and Analysis | | | |
| | Dinner SC4: Immunology for Immuno-Oncology | | | Dinner SC6: Advice on Putting Together an Integrated Summary of Immunogenicity | | | |

### CONFERENCE DISCOUNTS

**Alumni Discount – SAVE 20%:** CHI appreciates your past participation at the Immunogenicity and Bioassay Summit. As a result of the great loyalty you have shown us, we are pleased to extend to you the exclusive opportunity to save an additional 20% off the registration rate.

**Poster Submission - Discount ($50 Off):** Poster abstracts are due by September 21, 2018. 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.

**Group Discounts:** Special rates are available for multiple attendees from the same organization and for NIH/Government employees. For more information on group and government discounts contact Christopher Cardarelli at 781-247-1817.

**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.

**Alumni, Twitter, LinkedIN, Facebook or any other promotional discounts cannot be combined. Discounts not applicable on Event Short Courses.*

If you are unable to attend but would like to purchase the Immunogenicity and Bioassay Summit 2018 CD for $750 (plus shipping), please visit ImmunogenicitySummit.com.

**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 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 **1827F** when registering!

**Please refer to the Registration Code below:**

Cambridge HEALTHTECH Institute

A Division of Cambridge Innovation Institute

250 First Avenue, Suite 300
Needham, MA 02494
Healthtech.com
Fax: 781-972-5425