Well Characterized Biologics & Biological Assays

October 25-27, 2017
Rockville, MD
Hilton Rockville

ENSURE CMC SUCCESS AND EXPEDITE YOUR PRODUCT'S PATH TO MARKET BY OPTIMIZING PROTEIN CHARACTERIZATION STRATEGIES AND CMC BIOASSAY DEVELOPMENT

Improve your CMC programs by applying lessons from multiple case studies

Learn about regulatory expectations from the source by meeting with multiple FDA reviewers

Come and meet the following FDA Speakers

Top 10 Analytical Inadequacies in IND or BLA Submissions
Alfred Del Grosso, Ph.D.
Team Leader, Analytical Chemistry,
FDA/CBER/OCBQ/DBSQC

Regulatory Considerations on the Expedited Review Programs
Cara R. Fiore, Ph.D.
Microbiologist, Master Reviewer, Division of Vaccines and Related Products Application, Office of Vaccines Research and Review, Center for Biologics Evaluation and Research
U.S. FDA

Characterization of Fc-Fusion Protein Interactions with the Repertoire of Human Fc Receptors
Daniel Lagasse, Ph.D.
Center for Biologics Evaluation and Research
U.S. FDA

Regulatory Considerations for Antibody-Drug Conjugates and Case Studies
Wen Jin Wu, M.D., Ph.D.
Senior Investigator,
CDER, U.S. FDA

Simple NMR Methods for Evaluating HOS of Monoclonal Antibody Therapeutic Quinary Structure
Kang Chen, Ph.D.
Chemist
CDER, U.S. FDA

KNect365
Life Sciences

For up-to-date program information visit www.wcbbioassay.com

THE PREMIER FORUM FOR REGULATORY UPDATES AND CASE STUDIES ON WELL CHARACTERIZED BIOLOGICS & BIOLOGICAL ASSAYS

By attending, you will:

- **Gain practical advice** from multiple case studies that you can apply to your own projects
- **Hear unpublished, new data** from leading biologics drug developers
- **Get your regulatory questions answered** by meeting multiple FDA speakers
- **Accelerate your molecule development** by finding new analytical or bioassay technology applications

WELL CHARACTERIZED BIOLOGICALS

Advance your knowledge of analytical strategies, regulatory perspectives, and technology for protein and molecule characterization and comparability of biological products

Scientific Advisory Board:

John Alvino, Senior Manager, Global RA-CMC, GRAPSQA, AstraZeneca

Luke Arbogast, Ph.D., Research Chemist, Institute for Bioscience and Biotechnology Research, National Institute of Standards and Technology

Parastoo Azadi, Ph.D., Technical Director, Complex Carbohydrate Research Center, University of Georgia

Richard Cavicchi, Ph.D., Physicist, Bioprocess Measurements Group, National Institute of Standards and Technology

Darryl Davis, Ph.D., Associate Director, Analytical, Janssen R&D LLC

Zhenyu Gu, Ph.D., Scientist III, Global Analytical and Pharmaceutical Development, Alexion Pharmaceuticals

Suzanne Hudak, M.S., Scientist, Formulation Sciences, Medimmune

Nomalie Jaya, Ph.D., Principal Scientist, Analytical Sciences, Seattle Genetics, Inc.

Ho-Young Lee, Ph.D., Scientist, ADQC/Biological Technologies, Genentech, Inc.

Ranjini Kaushik, Ph.D., Senior Scientist, Attribute Sciences, Process Development, Amgen Inc.

Carol Shultz, Ph.D., Associate Principal Scientist, Merck & Co.

Renuka Sivendran, Ph.D., Principal Scientist, Amgen Inc.

Rosemary J. Versteegan, Ph.D., CEO, International Serum Industry Association

Xiaobin Xu, Ph.D., Staff Scientist, Analytical Chemistry, Regeneron Pharmaceuticals, Inc.

Santosh Yadav, Principal Scientist, Merck Manufacturing Division, Merck & Co.

Yi Yang, MSc., Senior Scientist, Genentech, Inc.

BIOLOGICAL ASSAYS

Apply new technologies and regulatory strategies to improve CMC bioassay development and validation for platform and complex/ emerging biologics

Scientific Advisory Board:

Souravi Ghosh, Ph.D., Senior Scientist Assay Innovation, Research & Clinical Bioanalytics, CSL Limited, Australia

Guoying Jiang, Ph.D., Associate Scientist, Analytical Development and Quality Control, Genentech, Inc.

Han Li, Principal Scientist, Bristol Myers Squibb

Kenneth R. Miller, Ph.D., Senior Scientist, Bioassay Development, Department of Analytical Sciences, Medimmune

Nadine M. Ritter, Ph.D., President and Analytical Advisor, Global Biotech Experts

Pin Yee Wong, Associate Director, Analytical Development and Quality Control, Genentech

Wei Zhang, Ph.D., Principal Scientist, Analytical Development, Biogen

MORE SPEAKERS, ADDITIONAL NETWORKING, MORE POSTERS, LARGER EXHIBIT HALL

New for 2017

- **Two Full Day Pre-Conference Workshops:**
  - Mass Spectrometry and Other Analytical Technology to Enable Protein and Molecule Characterization
  - An Introduction to Bioassay Development
- **New insights on FDA** expectations for Biosimilars
- **Co-located events** so you can cross-fertilize ideas with CMC analytical colleagues across product characterization and bioassay development. One registration fee provides access to both events, to help you connect critical issues in the development of both physiochemical and functional analytical methods

Event Highlights

- **More FDA and regulatory speakers** and perspectives
- **Case studies** with practical advice you can apply in your CMC programs, plus new data and lessons learned from an open information-sharing environment
- Shared **poster sessions**
- **Meet face-to-face** and build relationships with your peers at networking breaks and an evening reception
- **Luncheon roundtable discussions**
- **Larger exhibit hall** featuring Beckman Coulter, Caprion, Eurofins, KBI Biopharma, and more
- **Technology and Solutions Workshops** hosted by ProZyme, ThermoFisher Scientific, Bruker, and more

By the Numbers

30+ Case Studies and New Data Sessions

10+ Technology & Solutions Workshops

50+ Speakers

10+ Roundtable Discussions

For up-to-date program information visit www.wcbbioassay.com

PRE-CONFERENCE WORKSHOPS • WEDNESDAY, OCTOBER 25, 2017 • 9:00am-5:00pm

Workshop 1:
Mass Spectrometry and Other Analytical Technologies t o Enable Protein and Molecule Characterization

Workshop Overview

This multi-speaker workshop will begin with an introduction to an array of analytical technologies currently used. Attendees will then hear a diverse range of case studies and unpublished data discussing these relevant and useful analytical technologies for characterization.

Who should attend?

Anyone interested in analytical technology for characterization of proteins and molecules; including scientists currently using or wanting to learn more about NMR, various types of Mass Spectrometry and those involved in analytical R&D, CMC, Protein Analytical Chemistry, and mAb characterization.

Confirmed Workshop Presentations and Speakers:

Chairperson's Remarks
Zhenyu Gu, Ph.D., Scientist III, Global Analytical and Pharmaceutical Development, Alexion Pharmaceuticals

Using QC Friendly Mass Spectrometry to Quantitate the Critical Charge Variant from a Minor Component in Combination
Mingyan Cao, Ph.D., Senior Scientist II, Analytical Biochemistry, Medimmune

Applications of 2D NMR for Characterization of Monoclonal Antibody Therapeutics
Luke Arbogast, Ph.D., Research Chemist, National Institute of Standards and Technology

Mass Spec for Potency Testing of Adenovirus Vectors
Marta Germano, Ph.D., Associate Scientific Director, Janssen Vaccines

Analytical Technologies for Formulation Development and Characterization of Proteins and Molecules
Tudor Arvinte, Ph.D., Titular Professor of Biopharmaceutics, University of Geneva, *Switzerland;* Chairman, CEO, Therapeomic Inc.

More sessions to be announced soon!

Workshop 2:
Building a Better Bioassay: An Introduction to Bioassay Development

Workshop Outline

- Introductions & Schedule
- Why a Bioassay & Characterizing a 'well characterized' product
- Basic tools: Analyst training, documents, equipment, reagents, assay formats, cells
- Designing Bioassays Part I
- Cells
- Designing Bioassays Part II
- Regulatory Expectations
- Data Analysis/System Suitability and Acceptance Criteria
- Data Trending
- Supporting assay technologies
- Bioassay Transfer
- A global approach to bioassays: Outsourcing
- Case Studies
- Lessons Learned
- Questions & Discussion

Workshop Moderators:

Michael Merges, Director of Strategic Growth, Biologics Analytical Services , Catalent Pharma Solutions

Michael Sadick, Ph.D., Principal Scientist, Catalent Pharma Solutions

Who should attend?

Scientists, Managers and Directors in:

- CMC Bioassay Development, Assay Innovation
- Analytical R&D
- CMC
- Protein Analytical Chemistry
- Product Characterization
- Statistics
- Biological Development and Biological Technologies
- Bioanalytics
- Regulatory Affairs, QA/QC

MAIN CONFERENCE • THURSDAY, OCTOBER 26, 2017

7:00 *Coffee and Registration*

8:10 **Chairperson's Remarks**

Plenary Session

8:15

Physical or Functional: Which is the Most Important Analytical Characteristic of a Biotech or Biosimilar Product?
Nadine Ritter, Ph.D., Global Biotech Experts, LLC

8:45

Top 10 Analytical Inadequacies in IND or BLA
Alfred Del Grosso, Ph.D., Team Leader, Analytical Chemistry, **FDA/CBER/OCBQ/DBSQC**

FDA SPEAKER

9:15

Regulatory Considerations on the Expedited Review Programs
Cara R. Fiore, Ph.D., Microbiologist, Master Reviewer, Division of Vaccines and Related Products Application, Office of Vaccines Research and Review, Center for Biologics Evaluation and Research, **U.S. FDA**

FDA SPEAKER

Concurrent Technology Workshops

9:45

Overcoming the Challenges of Intact Biotherapeutics Characterization with Ultra-High Resolution Mass Spectrometers and the Latest in Automated Biopharmaceutical Software Package – Biopharma Compass 2.0

BRUKER

Attendees of this technology seminar will hear about the latest advancements in ultrahigh-resolution time-of-flight hardware and their application to the analytical challenges facing innovators and biosimilars characterization labs. Innovations in hardware, software and application-specific workflows will be highlighted. In particular, the use of MALDI- and LC-TOF hardware in combination, all acquired and visualized with a single, ease-to-use, 21CFR Part 11 compliant software package; Biopharma Compass 2.0. Several case studies involving monoclonal antibodies characterization will be presented to highlight: How high-confidence (high resolution) intact/subunit workflows improves labs productivity and; how automation of routine data processing tasks improves the system utilization time.

Jason Wood, Ph.D., Market Manager, **Bruker Daltonics Inc.**

Technology Workshop Available
For more information, contact Kristen Schott • kristen.schott@KNect365.com • 857-504-6685

10:15 *Networking Refreshment Break in the Poster & Exhibit Hall*

"This conference was very relevant with current events and trends. It provided a good arena for industry leaders to network and share ideas and best practices." – John Alvino, MedImmune

MAIN CONFERENCE • THURSDAY, OCTOBER 26, 2017

Well Characterized Biologics

NEW! Biological Assays

10:55

Chairperson's Remarks
Suzanne Hudak, M.S., Scientist, Formulation Sciences, **Medimmune**

Chairperson's Remarks

Chairperson's Remarks

Analytical Characterization Strategies for ADCs, Bispecifics, Fusion Proteins

11:00

Analytical Assay Development for Biopharmaceutical Proteins Using Automated Capillary Electrophoresis (CE) Western Blot CASE STUDY NEW DATA

This session discusses the use of CE Western blot (from Protein Simple) as applied in the analytical assay development for protein pharmaceuticals, including monoclonal antibodies and Fc-fusion proteins. It was a very useful tool for titer measurement in process intermediates, final drug product characterization, and host-cell-protein (HCP) impurity identification/quantitation. You'll hear about the possibility of a process control strategy from reviewing the percentages of molecular weight variants in a final purified Fc-fusion protein can be predicted from the size-based CE Western analysis on its cell culture harvest samples. A charge-based CE Western blot was also developed to monitor the isoform distribution for a monoclonal antibody during the cell culture process and for batch-to-batch consistency.

Dong Xu, Ph.D., Senior Scientist, Analytical Development, **Biogen Inc.**

11:30

Characterizing the Physiochemical Impact of Size Variants in an Antibody-Drug Conjugate CASE STUDY NEW DATA

Antibody-drug conjugates (ADCs) represent a unique class of drugs consisting of a monoclonal antibody (mAb) conjugated with cytotoxic small molecules through chemical linkers. Although the level of complexity and heterogeneity associated with ADCs can be challenging, ADCs can be well characterized using appropriate analytical tools to ultimately ensure patient safety and efficacy. This session presents a case study on the characterization of size variants for an engineered cysteine antibody (EC-mAb) conjugated to two pyrrolobenzodiazepine (PBD) dimer drugs via protease-cleavable linkers. High molecular weight (HMW) and low molecular weight (LMW) species were purified to a high degree of purity from size exclusion chromatography. These variants were characterized using a comprehensive set of analytical techniques. In this talk, a complete story on the physiochemical nature of the size variants will be presented for the PBD linked ADC and its drug intermediate mAb

Sunnie Kim, Ph.D., Senior Scientist, Analytical Sciences, **Seattle Genetics**

12:00

Late Breaking Presentation

Analytical Methods for Identification and Quantification of Host Cell Proteins

Host Residual DNA Testing: New Paradigms and New Techniques NEW DATA

The biologics manufacturer needs to demonstrate a safe level of host–residual DNA (hrDNA) in the purified drug. Instead of DNA extraction followed by qPCR we developed extraction-free methods where CHO-derived samples were protease-digested and directly subjected to qPCR or dPCR. We have also developed direct dPCR assays for Pichia and E. coli hrDNA. We show that in some ways dPCR is better than qPCR.

Musaddeq Hussain, Ph.D., Principal Scientist, **Merck & Co., Inc.**

Identification and Quantification of HCPs in mAbs, Recombinant Proteins and Biosimilars by Mass Spectrometry

Gel-free, label-free mass spectrometry (MS) enables identification and quantitation of total and individual HCP in biotherapeutic products, and represents an orthogonal method to ELISA. This session will present examples showing the use of semi-quantitative HCP discovery (LC-MS/MS) and absolute quantitation of HCP (LC-MRM/MS) as applied to monitoring of process changes, improvements, scale-up, batch uniformity, clearance, and comparison of Biosimilars vs. Innovators.

Laura McIntosh, Ph.D., VP Translational Research, Proteomics, **Caprion Biosciences Inc.**

Late Breaking Presentation

QbD and DoE Approaches to Bioassay Development

Quality by Design in the Bioassay Development Lab

QbD principles, which have traditionally been used in the context of biopharmaceutical manufacturing processes, can also be applied to bioassay development. This presentation will describe how QbD elements are being used for the development of bioassays that are included as part of lot release and stability testing programs.

Kenneth R. Miller, Ph.D., Senior Scientist, Bioassay Development, Department of Analytical Sciences, **Medimmune**

Use of DoE Approaches for Potency Assay Development

The antigen is a serine protease that can be deactivated upon antibody binding. In this presentation, we will share our experience implementing DoE for developing ELISA binding, enzymatic assay and cell based assay, which reflects three levels of MOA. As a part of ELISA binding assay development, using DoE to compare manual and automation will be discussed. In the end, we will compare testing results from these assays, which enable us to gain a deeper understanding of certain attributes and the MOA.

Xuan Gao, Ph.D., Scientist, Analytical Development and Quality Control – Biological Technologies, **Genentech**

A Case Study of Applying DOE and Automation into a Cell-based Neutralizing Antibody Assay CASE STUDY NEW DATA

BMS is spearheading immuno-cancer therapy with multiple biotherapeutics approved. One requirement for BLA application is neutralizing antibody (NAb) assay and cell-based functional NAb assay is highly recommended by all regulatory agencies. Although BMS has successfully developed, validated and tested clinical samples for all approved biotherapeutics, it turned out to be a pain to transfer these cell-based assay to CRO, due to sensitive cells as critical reagents and much complicated assay set up. One way to circumvent the hurdle of complicated assay transfer is automation. In this case study, we will show how DOE and automation is applied during the assay development for a cell-based functional NAb assay. This not only standardizes cell-based NAb assay development, simplifier assay validation but will also greatly facilitate assay transferring.

Weifeng Xu, Ph.D., Senior Research Investigator, **Bristol-Myers Squibb**

MAIN CONFERENCE • THURSDAY, OCTOBER 26, 2017

Luncheon Roundtable Discussions in Poster and Exhibit Hall

12:30

Table A: Biosimilar Comparability Strategies: Effectively Comparing Reference Product to Biosimilars
Moderators: **Santosh Yadav,** Principal Scientist, Merck Manufacturing Division, **Merck & Co.** and **Renuka Sivendran, Ph.D.,** Principal Scientist, **Amgen Inc.**

Table B: Control Strategies for Host Cell Proteins
Moderator: **Nadine Ritter, Ph.D., Global Biotech Experts, LLC**

Table C: Setting Specifications Based on Patient Exposure
Moderator: **Elisabeth Krug, Ph.D.,** rincipal Research Scientist, **Eli Lilly and Company**

Table D: Bioassays for Biosimilars
Rajani Srikakulam, Ph.D., Principal Scientist, **Adello Biologics**

Table E: Topic TBA
Moderator:
Christopher Sucato, Charles River Labs

Well Characterized Biologics

NEW! Biological Assays

1:40

Chairperson's Remarks
Nomalie Jaya, Ph.D., Principal Scientist, Analytical Sciences, **Seattle Genetics**

Chairperson's Remarks
Luke Arbogast, Ph.D., Research Chemist, **National Institute of Standards and Technology**

Chairperson's Remarks
Wei Zhang, Ph.D., Principal Scientist, Analytical Development, **Biogen**

Analytical Characterization Strategies for ADCs, Bispecifics, Fusion Proteins

Strategies for Higher Order Structure

Lifecycle Management of Bioassays and Assay Changes to Commercial Products

1:45

Analytical Characterization Challenges of Site-Specific Antibody Drug Conjugates CASE STUDY NEW DATA

Conventional antibody drug conjugates (ADC) are usually heterogeneous mixtures of conjugated species. Site specific ADCs with near homogenous composition often show advantages over conventional ADCs, but also present unique challenges. This presentation will describe a case study of the analytical challenges we encountered with site-specific ADCs from two different conjugation techniques.

Lawrence Chen, M.S., Principal Scientist, **Pfizer, Inc.**

Simple NMR Methods for Evaluating HOS of Monoclonal Antibody Therapeutic Quinary Structure FDA SPEAKER

Correctly folded protein higher order structure (HOS), including secondary, tertiary, quaternary and quinary structures, is crucial for protein drug quality. For large multi-domain protein like monoclonal antibody (mAb), its oligomer can have quinary structure, association of its monomeric quaternary structure. Here, several commonly available analytical methods, i.e., size-exclusion-chromatography (SEC) FPLC, dynamics light scattering (DLS), NMR and multivariate analysis, were combined with in situ enzymatic cleavage to yield a complete profile of mAb HOS and comparable metrics. Rituximab and infliximab were chosen for method evaluation because both IgG1 molecules are known to be homologous in sequence, superimposable in Fab crystal structure and identical in Fc structure. However, herein the two are identified to be significantly different in quinary structure in addition to minor secondary structure differences. All data collectively showed rituximab was mostly monomeric while infliximab was in mono-oligomer equilibrium driven by its Fab fragment. This session with review the studies and discuss the analysis using the new in-situ enzymatic digestion method holds potential in identifying structural differences on larger therapeutic molecules using NMR.

Kang Chen, Ph.D., Chemist, **CDER – FDA**

Lifecycle Management for Bioassay Development and Validation

Lifecycle management for bioassay development starts with procedure design and continues through validation based on QbD. The concept of QbD is understood as a systematic approach that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management (ICH Q8). An overview of variability and measurement uncertainty to align decisions with results generated by a procedure will be presented.

Steven Walfish, Principal Science & Standards Liaison, **United States Pharmacopeia (USP)**

2:15

Late Breaking Presentation

CD Spectroscopy of Protein-Dye Complexes as a Characterization Tool for Protein Higher Order Structure

CD spectroscopy plays an important part in the development of protein pharmaceuticals, as a means to examine purified proteins for structural integrity and proper folding, and also to study relative conformational stabilities in response to changing pH, ionic strength, and other formulation variables. During production of biological prodsucts, CD spectroscopy can provide a non-invasive and non-destructive means of monitoring stability and checking batch-to-batch consistency of the drug product. CD spectroscopy in the near-UV wavelength region provides a tertiary structure fingerprint, including information on aromatic residues and disulphide bridges. This session will discuss how aromatic dyes or similar compounds can serve as probes of protein higher order structure, what these changes show, and the overall beneficial effects of the method.

Christopher Sucato, Ph.D., Senior Scientist, Biologics/Biophysical Characterization, **Charles River Laboratories**

Change or Replace? Lifecycle Management of Bioassays for Commercial Products CASE STUDY

Case studies will be presented to discuss implementing changes to bioassays already approved for commercial products. The focus will be on making decisions on whether to make modifications to the existing assay, or to develop a new, better assay.

Wei Zhang, Ph.D., Principal Scientist, Analytical Development, **Biogen**

MAIN CONFERENCE • THURSDAY, OCTOBER 26, 2017

Concurrent Technology Workshops

2:45

Glycans Before Lunch: Rapid N-Glycan Sample Preparation Workflows for Liquid Chromatography and Capillary Electrophoresis Platforms

PROzyme Advancing Glycosciences

Glycosylation is frequently a critical quality attribute of biotherapeutics, making the characterization of N-glycans an essential part of the development process. We present a rapid N-glycan sample preparation platform with a choice of labels for LC, LC-MS and CE applications. The Gly-Q CE platform enables relative N-glycan quantification for up to 96 cell culture samples within a single workday.

Aled Jones, Ph.D., Senior Product Manager, **ProZyme**

Robust and Simple Potency Bioassays for Biologics and Biosimilars

Jane Lamerdin, Ph.D., Director R&D, **DiscoverX Corp.**

DiscoverX

3:15

Networking Refreshment Break in the Poster & Exhibit Hall

Well Characterized Biologics

Analytical Methods for Identifying, Monitoring and Controlling Product and Process Variants and Impurities

3:45

Analytical Methods in Development: Robust Strategies for Charge Variants, Size-Exclusion Methods and other Methods

NEW DATA

Since its implementation, Quality by Design (QbD) has become an integral part of the pharmaceutical product development process. More and more, those principles also appy to analytical method development to ensure method appropriateness and robustness. Case studies for development approaches across different analytical techniques will be shared.

Elisabeth Krug, Ph.D., Principal Research Scientist, **Eli Lilly and Company**

4:15

Leveraging a Mass Spectrometry Based Multi-Attribute Method Platform for Monitoring Product Variants and Impurities

CASE STUDY NEW DATA

Current paradigms for monitoring biopharmaceutical variation during production and processing call for the use of multiple analytical platforms. The traditional methods report an indirect measure of a limited number of attributes per assay. A mass spectrometry-based multi-attribute method (MAM), however, has the power to evaluate multiple critical quality attributes (CQA) in a single assay with the additional advantage of providing site-specific information. The MAM is being heavily explored in the industry to streamline the quality control process and potentially replace multiple analytical methods. The MAM platform has the potential to reduce both analytical turn-around time and the use of multiple workflows and thus may reduce the analytical burden on the quality control lab. Co-Authors of this data are John Schiel, Research Chemist, NIST/IBBR; Richard Rogers, Scientist 4, Just Biotherapeutics

Trina Mouchahoir, Ph.D., Research Chemist, Biomolecular Measurement Division, **National Institute of Standards and Technology (NIST)**

4:45

Characterization of Antibody Charge Variants Induced by Metal-Catalyzed Oxidation

NEW DATA

Characterization of charge variants is important for evaluating product quality attributes of monoclonal antibodies, and for ensuring the safety and efficacy of antibody drug products. Recently, we reported a correlation between formation of charge variants and metal-catalyzed oxidation during production and storage of monoclonal antibodies. However, to date, the charge variants and the related mechanism have not been elucidated in the literature to explain the observed correlation. In this work, charge variants of an antibody stressed by metal-catalyzed oxidation were fractionated by ion exchange chromatography. A wide range of physicochemical assays was subsequently applied to characterize these fractions at both protein and peptide levels. Several novel charge variants were identified. These findings help explain the observed correlation and provide valuable information for a critical assessment of the induced charge variants. This work also demonstrates that metal-catalyzed oxidation represents a new degradation mechanism for inducing charge heterogeneity on monoclonal antibodies.

Yi Yang, M.S., Senior Scientist, **Genentech, Inc.**

NEW! Biological Assays

CMC Biological Assay Case Studies

MoA-reflective Bioassays for a Monoclonal Antibody Targeting a T Cell Co-Stimulatory Receptor

CASE STUDY

Generating anti-tumor immune responses with antibodies that activate T-cell co-stimulatory receptors while at the same time modulating interactions with Fcγ receptors is a promising approach in cancer immunotherapy. We have characterized a monoclonal antibody (mAb) with the capacity to modulate FcγR interactions and target a co-stimulatory T cell receptor. For assessment of a molecule with multiple mechanisms of action (MoA), it is important to consider characterization strategies that fully capture the functional capability of the therapeutic protein. Challenges and approaches to design relevant in-vitro assays for therapeutic antibodies with complex MoA will be presented.

Ganesh Shankarling, Ph.D., Scientist, Molecular and Analytical Development, Bioassay Center of Excellence, **Bristol-Myers Squibb**

Development of a Murine Reporter Cell Line System to Support Potency Assays Targeting Immuno-Modulatory Receptors

CASE STUDY

A murine reporter cell line system was designed to have a broad application to Immuno-Modulatory Receptors potency assays. In the system, a 3A9 T cell line was engineered with IL2-luciferase and co-expresses an IMR, and a LK35.2 B cell line that expresses inhibitory receptor ligand. Bridging study demonstrated 3A9 cell line system has comparable suitability to equivalent mammalian cell line system. Further study showed the system possessed superior linearity (25%-200%), intermediate precision (GSD 4.3%), sensitivity and robustness.

Ray Zhang, Ph.D., Associate Principle Scientist, Biologics and Vaccines Analytical Development, **Merck**

Late Breaking Presentation

5:15

Networking Cocktail Reception in Poster and Exhibit Hall

MAIN CONFERENCE • FRIDAY, OCTOBER 27, 2017

7:00 *Coffee and Registration*

7:15 **Breakfast Technology Workshops Available for Sponsorship** For more information, contact Kristen Schott • kristen.schott@KNect365.com • 857-504-6685

8:05 **Chairperson's Remarks** **Carol Shultz, Ph.D.,** Associate Principal Scientist, **Merck & Co.**

Plenary Session: FDA Perspective – Physical and Functional Characterization

8:10 

Characterization of Fc-Fusion Protein Interactions with the Repertoire of Human Fc Receptors
Daniel Lagasse, Ph.D., Center for Biologics Evaluation and Research, **U.S. FDA**

FDA SPEAKER

8:40 

Biosimilars: Update on FDA Scientific and Regulatory Expectations for Characterization and Approval
Emily Shacter, Ph.D., Independent Consultant, **ThinkFDA, LLC**

NEW DATA

9:10 

Regulatory Considerations for Antibody-Drug Conjugates and Case Studies
Wen Jin Wu, M.D., Ph.D., CDER, FDA

FDA SPEAKER

Concurrent Technology Workshops

9:40 **Technology Workshop Available**
For more information, contact Kristen Schott • kristen.schott@KNect365.com • 857-504-6685

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10:10 *Networking Refreshment Break in the Poster & Exhibit Hall*

Well Characterized Biologics

10:40 **Chairperson's Remarks**

Case Studies of Protein Characterization and Product Comparability

10:45 **Overview of Analytical Characterization Methods Used to Demonstrate Comparability of Hepatitis A Vaccine**

CASE STUDY NEW DATA

ICH Q5E recommends that chances to manufacturing processes be evaluated via comparability to ensure the quality, safety and efficacy of drug product. Comparability evaluations can be performed by comparing assay results against predefined acceptance criteria/alert levels without requiring clinical trials. A case study focusing on characterization assays performed for the assessment of comparability of Hepatitis A vaccine will be presented.

Mary Latza, M.S., Associate Director, Technical Services, **Merck & Co., Inc.**

NEW! Biological Assays

Chairperson's Remarks
Carol Shultz, Ph.D., Associate Principal Scientist, **Merck & Co.**

Bioassay Development for Biosimilars and Complex Molecules

Functional Assays for Similarity Assessment of Biosimilars
Rajani Srikakulam, Ph.D., Principal Scientist, **Adello Biologics**

MAIN CONFERENCE • FRIDAY, OCTOBER 27, 2017

Well Characterized Biologics

Case Studies of Protein Characterization and Product Comparability
(continued)

11:15 **Comparability Assessment of an Antibody-drug Conjugate (ADC) for Entry into Late-stage Clinical Trial** CASE STUDY

In preparation for commercial launch of an ImmunoGen ADC, changes were made to manufacturing processes of the antibody intermediate (Ab), the ADC drug substance (DS) and ADC drug product (DP). Antibody manufacturing changes were made to increase antibody titer, improve antibody manufacturing robustness, and change antibody storage buffer. DS and DP manufacturing processes were scaled up. The comparability strategy for inclusion of this ADC into PIII clinical studies will be discussed.

Paul Weisbach, Scientist I, **ImmunoGen, Inc**

11:45 **Case Studies of USP's Compendial Approach to the Analysis of Biotherapeutics** CASE STUDY NEW DATA

The USP Global Biologics department develops monographs and associated general chapters in the area of biotherapeutics. Various methodologies are used for the purposes of establishing identity, strength, quality, and purity of biotherapeutics. Chromatography, electrophoresis, and bioassays are examples of methods used to address key quality attributes covered in USP standards.

Kevin Carrick, Ph.D., Senior Scientific Liaison, Global Biologics, **United States Pharmacopeia**

Biological Assays

Bioassay Development for Biosimilars and Complex Molecules
(continued)

11:15 **Bioassays Empower Biologics Development**

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

11:45 **Near-universal Equivalence Bounds for Similarity in Bioassays**

David Lansky Ph.D., President and Principal Statistician, **Precision Bioassay, Inc.**

Luncheon Roundtable Discussions in Poster and Exhibit Hall

12:15

Table A: Lessons Learned from Comparability Assessments of an Established Commercial Vaccine Product
Moderator: **Mary Latza, M.S.,** Associate Director, Technical Services, **Merck & Co., Inc.**

Table B: Statistical Control Charting for Bioassays
Kenneth R. Miller, Ph.D., Senior Scientist, Bioassay Development, Department of Analytical Sciences, **Medimmune**

Table C: Demonstrating Comparability by Analytical and Biological Assays
Moderator: **Yi Yang, M.S.,** Senior Scientist, **Genentech, Inc.**

Table D: Automation of Bioassays
John Lehrach, Research Scientist, Leads Discovery & Optimization, **Bristol-Myers Squibb**

Table E: Strategies for BLA, enabling ADC Characterization
Moderator: **Nomalie Jaya, Ph.D.,** Principal Scientist, Analytical Sciences, **Seattle Genetics, Inc.**

Table F: ADC Regulatory Considerations
Moderator: **Wen Jin Wu, M.D., Ph.D.,** Senior Investigator, **CDER, US FDA**

1:25 **Chairperson's Remarks**

Chairperson's Remarks

Analytical Strategies for Stability Studies for Diverse Products

1:30 **Considerations for In-Use Stability Studies for Monoclonal Antibody Therapeutics** CASE STUDY

Design and execution of the relevant conditions for in-use stability studies for parenteral biological products are critical for ensuring drug efficacy and patient safety. The study should simulate the potential steps and hold times from the start of product preparation through administration of the product. Results from the study are used to determine the relevant information needed for the commercial package insert, such as allowable hold times and acceptable diluents used during administration. This presentation will focus on strategy used for designing an in-use study in the context of expectations from regulatory authorities. A case study on a monoclonal antibody for intravenous infusion will be presented. Stability of the drug product in different diluents and hold times will be discussed, as well as the effect of degradation products from the diluent itself.

Suzanne Hudak, M.S., Scientist**, Medimmune**

Method Bridging and Method Tech Transfer for Bioassays

Strategies for Bridging Late Phase Cell-Based Potency Assays CASE STUDY

Potency assays are one of several analytical methods used to evaluate the functional integrity of biological drug products. Analytical methods are required to assess product quality attributes for biotherapeutics prior to product release. During the lifecycle of a biological product, new or revised analytical methods may be introduced as a replacement to the current method(s) for providing increased efficiency, enhanced quality, and/or greater robustness. In order to replace an analytical method during late stage and post-commercialization, regulatory agencies expect the sponsors to conduct robust method bridging studies to evaluate and demonstrate equivalence between the current and new method(s). Conventionally, method bridging studies include testing of release and stability samples and establishing comparability over time. The extent and duration of the comparability study is largely determined by the drug product's stage and the nature of analytical method. Method comparability for potency assays remains challenging due to the complexity of the methods themselves and the functional attribute (relative potency) that needs to be bridged. A case study of late phase method bridging between two cell-based potency assays will be presented. Criteria for establishing comparability as well as strategies for, and challenges to, method replacement at different product phases will be discussed.

Amy Teale, Ph.D., Senior Analytical Scientist, **Regeneron Pharmaceuticals**

MAIN CONFERENCE • FRIDAY, OCTOBER 27, 2017

Well Characterized Biologics

Biological Assays

2:00

PANEL DISCUSSION: Defining Minimum Requirements for Stability in a Phase Appropriate Fashion (including late stage)

Moderator:

Ranjini Kaushik, Ph.D., Senior Scientist, Attribute Sciences, Process Development, **Amgen Inc.**

Panelists:

Shawn Novick, Senior Director of Quality Control, **Seattle Genetics**

Denise Kingsbury, M.S., Associate Scientist, **MedImmune**

A Road Map for Addressing Changes on a Validated Reporter Gene Bioassay CASE STUDY

Improvement to any validated bioassay is a routine activity in bioassay life cycle management to reflect the "c" in cGMP environment. Cells, as critical reagent in bioassay, tend to behave differently along passaging, which impact assay performance. Cell maintenance is labor intensive, time consuming and costly. In this case study, frozen cells were directly used in a validated bioassay after thawing (ready-to-use) to replace freshly harvested cells (fresh harvest). In order to evaluate the equivalency between fresh harvest and ready-to-use, a road map was designed to include: 1) determination of optimal freezing medium; 2) demonstration capability of frozen cells from representative cell banks created at different passages, 3) verification of assay performance(assay range and other critical assay parameters) with linearity samples and cell banks created at different passages; 4) confirmation of assay accuracy, precision and linearity with cells frozen at early passage; and 5) robustness study. Data generated from this design suggested that ready-to-use and fresh harvest are equivalent and can both be used in the validated bioassay. More data are to be generated on side-by-side in GMP sample testing for the transition.

Xin Li, Scientist II, Global Technical Operations, **AstraZeneca**

Concurrent Technology Workshops

2:30

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3:00 *Networking Refreshment Break in the Poster & Exhibit Hall*

Well Characterized Biologics

Biosimilar Characterization and Comparability

Biological Assays

Potency Assays: Automation, Statistics & Critical Reagents

3:30

Structural and Functional Studies of Infliximab and ABP 710 Biosimilars

ABP 710 is being developed as a biosimilar product to infliximab (Remicade®). Infliximab and ABP 710 are chimeric human-murine Immunoglobulin G Type 1 (IgG1) monoclonal antibodies that bind and neutralize human tumor necrosis factor alpha (TNFa). Infliximab is produced in murine hybridoma cells (Sp2/0) and ABP 710 is produced in Chinese hamster ovary (CHO) cells. Demonstrating analytical similarity is critical for the approval of a biosimilar product. Therefore, structural and functional studies of ABP 710 and infliximab were performed to demonstrate that ABP 710 is analytically similar to infliximab. CASE STUDY NEW DATA

Renuka Sivendran, Ph.D., Principal Scientist, Biosimilars Process Development, **Amgen Inc.**

Additional Contributors: **Ramsey Saleem, Palanisamy Kanakaraj, Cynthia Li, Shawn Cao, and Jennifer Liu.**

Scientific and Statistical Approaches for Developing Potency Assays for Bispecific Antibodies

Maroun Beyrouthy, Ph.D., Research Scientist, Bioassay Group, **Eli Lilly and Company**

4:00

Using Stability Descriptors and Biophysical Predictors for Successful Biosimilar Formulation Development and Characterization CASE STUDY

Biosimilar formulation and drug product development presents a unique challenge whether to copy the reference product composition or to develop a rational alternate composition. The landscape of formulation and drug product development for biosimilars which includes FDA guidance, Intellectual property aspects and life cycle management will be reviewed. This presentation will discuss how DLS-couple Raman Spectroscopy (Zetasizer Helix) can be effectively utilized to characterize the degradation profile and overall stability of a biosimilar antibody formulation compared to reference product. The presentation will briefly touch on another case study wherein the liquid formulation for a biosimilar product was developed from a unique biophysical predictors derived from biophysical methods including light scattering (DLS, SLS) and thermal methods (DSC). The developed alternative formulation was tested and compared to reference product for stability descriptors, namely subvisible and submicron particle profile and viscosity. In summary both case studies will highlight how formulation development, characterization and stability assessment for biosimilars can be achieved by use of orthogonal biophysical characterization tools.

Hiten Gutka, Ph.D., Principal Scientist, Formulation Development, **Oncobiologics Inc.**

Accelerating Potency Bioassay Delivery by Leveraging Automation and Cellular Assay Platforms CASE STUDY

Leads Discovery & Optimization (LDO) Department within BMS has created a centralized Core Bioassay Group (CBG) to bridge drug discovery and bioassay development, as well as, transfer target knowledge to GMS collaborators. Efficient potency bioassay workflows have been developed to streamline go/no go decisions for selecting and validating the right "fit for purpose" bioassay platforms with proper MOA linkage. Multiple case-studies will be highlighted to demonstrate how CBG leveraged automation technology to accelerate key deliverables and help reduce the timeline from drug discovery to bioassay optimization, including case studies of how LDO transferred potency bioassays to QC lab for product quality testing.

John Lehrach, Research Scientist, Leads Discovery & Optimization, **Bristol-Myers Squibb**

4:30

New Techniques for Characterization of Glycoprotein Drug Products

We have developed a platform for the analysis of glycoproteins by integrating glycomics and glycoproteomics in a single one-pot experiment through the permethylation of glycopeptides and their tandem mass spectrometry analysis. The proposed methodology has the potential to accelerate glycoproteomics research and to make it accessible to the pharmaceutical industry.

Parastoo Azadi, Ph.D., Technical Director, Complex Carbohydrate Research Center, **University of Georgia**

Strategies for Critical Reagent Management for Potency Assays CASE STUDY

Vineetha Jayasena, Ph.D., Principal Scientist, **Amgen**

*Close of Conference – **See you in 2018!***

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