Cambridge Healthtech Institute's 8th Annual

Biotherapeutics Analytical Summit

March 20-24, 2017
Hyatt Regency • Bethesda, MD

Empowering Innovation with the Right Tools & Techniques

MARCH 20-21
Method Development Qualification & Validation

MARCH 21-22
Advances in Characterization Methods & Approaches

MARCH 21-22
Process Analytics & Characterization

MARCH 23-24
Comparability & Biosimilarity

Training Seminars
- Current Issues in Product & Process Impurities for Biotech and Biosimilar Products
- Regulatory Requirements Across the Product Development Lifecycle
- Introduction of Cell-Based Bioassay & Quantitative Control of its Performance

Short Courses
- Particles in Biotherapeutics: Characterization & Impact
- The Multi-Attribute Method (MAM) for Improving Product and Process Development
- New Analytical Approaches & Strategies for Comparability and Biosimilarity
- Glycobiology of Therapeutic Antibodies

Featured Speakers
- Alain Beck, Ph.D. Senior Director, Analytical Chemistry, NBEs, Center d’Immunology Pierre Fabre
- Michael Butler, Ph.D. CSO, National Institute for Bioprocessing Research and Training (NibRT)
- John Schiel, Ph.D. Research Chemist, Bioanalytical Chemistry, NIST
- Marjorie Shapiro, Ph.D. Chief, Laboratory of Molecular and Developmental Immunology, CDER, FDA

Click Here to Register Online! Biotherapeutics AnalyticalSummit.com
# Conference-at-a-Glance

<table>
<thead>
<tr>
<th>Date</th>
<th>MARCH 20-21</th>
<th>MARCH 21-22</th>
<th>MARCH 23-24</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product Characterization Stream</strong></td>
<td>Method Development, Qualification &amp; Validation</td>
<td>Advances in Characterization Methods &amp; Approaches</td>
<td>Comparability &amp; Biosimilarity</td>
</tr>
<tr>
<td><strong>Training Seminars</strong></td>
<td>TS</td>
<td>TS</td>
<td>TS</td>
</tr>
</tbody>
</table>

## MONDAY, MARCH 20 & THURSDAY, MARCH 23

### Dinner Short Courses

**Separate Registration Required**

**Monday, March 20, 2017, 6:00 - 8:30 PM**

**SC1: Particles in Biotherapeutics: Characterization & Impact**

Instructors: Dean Ripple, Ph.D., Supervisory Physicist, Bioprocess Measurements Group, National Institute of Standards and Technology
Srivalli Telikepalli, Ph.D., Research Chemist, Biomolecular Measurement, National Institute of Standards and Technology

This short course will give an introduction to current issues surrounding particle formation & characterization in biotherapeutics. Regulatory expectations provide the context of why particle loads are characterized and controlled. The basics of why and how proteins can aggregate will be presented along with a discussion of other particle types. An overview of the recent technology to accurately characterize various classes of aggregates and particles will be discussed. Studies from the current literature will be used to highlight various key points throughout the course.

**SC2: The Multi-Attribute Method (MAM) for Improving Product and Process Development**

Instructor: Richard Rogers, Ph.D., Scientist 4, Just Biotherapeutics

During biotherapeutic development, it is necessary to monitor properties of the therapeutic molecule and formulation that have been identified as critical quality attributes (CQAs) for product safety and efficacy. In particular, the industry is seeking to monitor post-translational modifications (PTMs), glycosylation profiles, and excipients with both UV and mass data by implementing multi-analyte or so-called Multi Attribute Methods (MAMs). MAMs have the potential to replace several conventional electrophoretic and chromatographic methods currently used in Quality Control to release therapeutic molecules. This course takes a practical look at the fundamentals of MAM in analytical process development, examples of typical data analysis and how the technology is being implemented to improve product and process understanding.

**THURSDAY, MARCH 23, 2017, 6:00 - 8:30 PM**

**SC3: New Analytical Approaches & Strategies for Comparability and Biosimilarity**

Instructors: Hans-Martin Mueller, Ph.D., Director, BioProcess Development, MSD Merck
David Wylie, Ph.D., Principal Scientist, Sterile Process and Analytical Development, Merck Research Labs

Providing convincing comparability studies is a key success factor for the filing of novel biologics. This is even more important for the steadily growing new field of biosimilars and biobetters. In this case, comparability studies are combined with demonstrating similarity. For a proper planning of novel or biosimilar development programs, it is important to understand the development costs, timelines and the authoring of CMC regulatory sections. The analytical characterization of comparability and similarity studies will form the cornerstone for each successful marketing authorization application of these products. This short course will be about analytical development and its challenges, technical hurdles, BLA authoring, timelines and costs. Participants will be introduced to state-of-the-art analytical comparability/similarity strategies, leading to a smooth and efficient IND/BLA application and approval.
Cambridge Healthtech Training Seminars offer real-life case studies, problems encountered and solutions applied, and extensive coverage of the basic science underlying each topic. Experienced Training Seminar instructors offer a mix of formal lectures, interactive discussions and activities to help attendees maximize their learning experiences. These immersive trainings will be of value to scientists from industry and academic research groups who are entering new fields—and to those working in supporting roles that will benefit from an in-depth briefing on a specific aspect of the industry.

**MONDAY, MARCH 20, 8:30 AM - 5:30 PM & TUESDAY, MARCH 21, 8:30 AM - 12:30 PM**

**TS1: Current Issues in Product & Process Impurities for Biotech and Biosimilar Products**

*Instructor: Nadine Ritter, Ph.D., President & Senior Analytical Advisor, Global Biotech Experts, LLC*

This class will provide an introduction to the current and emerging concerns for process and product impurities in biologically-derived products, and the analytical strategies necessary to address them. It will provide a comprehensive overview of the regulatory expectations for characterization and control of impurities throughout product development. It will illustrate current analytical practices for assessing host cell proteins, host cell DNA, and teachable, as well as product degradants such as aggregates, subvisible and visible particles. It will also highlight strategies for process and product comparability studies with focus on comparing the types and levels of impurities. Strategies for establishing appropriate specifications on process and product related impurities will be discussed, and the current expectations on analytical method lifecycle elements (qualification, validation, verification, tech transfer, and method bridging) will be presented. Finally, the risk of inadequate quality practices in analytical R&D labs generating these critical sets of impurity data will be emphasized. Topics to be covered include:

- Why do impurities in biologically-derived products present a safety risk different from chemical drug impurities?
- What are the specific global regulatory documents that apply to biological product impurities?
- What are the current expectations for characterization and comparability of product and process impurities?
- Which analytical methods are appropriate for analysis of process-related impurities vs product-related impurities?
- What are the emerging best practices for host cell protein analysis? Subvisible and visible particle analysis?
- What key elements in the lifecycles of compendial vs non-compendial methods?
- What business risks are posed by generating critical R&D analytical data without suitable quality practices?

**TUESDAY, MARCH 21, 1:45 PM - 6:00 PM & WEDNESDAY, MARCH 22, 8:30 AM - 5:30 PM**

**TS2: Regulatory Requirements across the Product Development Lifecycle**

*Instructor: Christina Vessely, Ph.D., Senior Consultant, Biologics Consulting Group*

The successful development of a pharmaceutical product requires not only good science, but also compliance with FDA regulatory expectations. This course will include a comprehensive review of the Chemistry, Manufacturing and Controls (CMC) section of regulatory filings, with a focus on phase appropriate requirements. The level of detail that must be included in the filing will be discussed as well as systems and controls that must be in place in the manufacturing setting. Topics such as process development, analytical development, Good Manufacturing Practices (GMP) and Good Laboratory Practices (GLP) will be discussed in the context of the stage of drug development. Regulatory strategies for navigating the path to approval will also be discussed. This course is intended to provide participants from all facets of the pharmaceutical and biotech industry with a broad understanding of regulatory requirements across the product development lifecycle.

Topics to be covered include:

- The Evolution of Drug Compliance in the US
- FDA Structure and Function
- The Product Development Timeline from IND to Commercialization
- Good Laboratory Practice
- Good Manufacturing Practice
- Compliance across the Product Development Lifecycle
- The CMC Section of the Initial IND
- Meetings with FDA During Drug Development
- The BLA, NDA and Beyond

**THURSDAY, MARCH 23, 8:30 AM - 5:30 PM & FRIDAY, MARCH 24, 8:30 AM - 12:00 PM**

**TS3: Introduction of Cell-Based Bioassay and Quantitative Control of Its Performance**

*Instructor: Liming Shi, MA, MSc, ADMET Certificate, Senior Group Leader, Bioassay Development, Pfizer, Inc.*

This Training Seminar will focus on fundamentals of cell-based bioassays and basic statistical methods that are routinely applied in bioanalytical laboratories. Covered topics will include mechanisms and principals of cell-based bioassays; study designs during assay development and optimization; cell-based bioassay validation and regulatory guidance; statistical process control during life cycle of cell-based bioassays.

Topics to be covered include:

- Uniqueness of cell-based bioassay
- Fundamental terms and concepts of biostatistics
- Basic bioanalytical measurements and calculations
- Cell-based bioassay development and validation
- Quality control of cell-based bioassay performance
- Comparative studies during method development and validation

**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.
MONDAY, MARCH 20 – TUESDAY, MARCH 21

Developing Fit-for-Purpose Methods throughout the Product Lifecycle

METHOD DEVELOPMENT DURING EARLY PHASE PROGRAMS

10:50 Development of a High Throughput HILIC-CAD Method to Quantify Trisulfides in Monoclonal Antibodies
Christopher Cornell, Msc., Technical Development Scientist, Protein Analytical Chemistry, Genentech, Inc.

In early drug development it is important to reduce costs and move quickly from candidate selection to the clinic. Approaches to streamline method development and qualification using risk based and QbD approaches will be presented.

11:20 LC-MS Multi-Attribute Methods for Non-mAb Protein Therapeutics – Streamlined Method Development Aligned with Clone Selection
Matt Taylor, Ph.D., Senior Scientist, Analytical Development, Shire
Multi-attribute LC-MS peptide mapping methods provide comprehensive characterization of protein therapeutics, and offer numerous benefits for the analytical support of process development. However, significant time and efforts are required to develop these methods. This talk will describe a case study where the development of a multi-attribute LCMS peptide map was simplified by aligning assay development with the analytical support of cell line development and clone selection.

11:50 A Streamlined Approach to Qualification of Platform Analytical Methods for Early-Phase Programs
Ruth Frenkel, Scientist I, Analytical Development, Biogen
Method qualifications in Biogen have historically followed a “one-size-fits-all” approach, closely adhering to the experiments recommended in ICH Q2(R1). A case study will be presented on how we have streamlined the qualifications for platform methods by leveraging the extensive data set generated from historical method qualification reports across multiple mAb programs, applying a phase-appropriate risk-based approach, and using Design-of-Experiments (DOE) to minimize the number of experiments needed to demonstrate that the platform method is fit for purpose for a new mAb.

12:20 pm Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:50 Session Break

METHOD DEVELOPMENT AND QUALIFICATION FOR NOVEL AND CHALLENGING PRODUCTS

1:45 Method Development and Qualification for Antibody-Drug Conjugates
Jim Qingping Jiang, Ph.D., Principal Scientist, Bio-Therapeutics Analytical RD, Pfizer
Antibody-drug conjugates (ADCs) are complex molecules comprised of three components: a monoclonal antibody with targeting abilities, a linker, and a small-molecule payload with cytotoxicity. Various conjugation chemistry techniques, including conventional conjugations and site specific conjugations, have been commonly used. However, each technique and ADC imposes different challenges to analytical method development. This presentation examines analytical challenges encountered during development of ADCs, as well as the analytical strategy for the isolation and characterization of ADCs.

2:15 Development and Verification of a High Resolution LC-MS Method for Quantitation of Antigens and Known Host Cell Proteins in Vaccine Products
Tim Guo, Ph.D., Senior Scientist, Analytical Development, Novavax
Accurate protein quantitation is important for vaccine product development. Low protein concentration and presence of multiple components may limit the applicability of spectroscopic techniques such as A280 or binding methods such as SRID or ELISA which require the generation of specific antibody reagents. Here we present the development and verification of a high-resolution LC-MS method for quantitation of antigens and host cell proteins in vaccine products.

2:45 Biologic Stability Cranked up to 11
Candi Warner, Field Application Scientist, Unchained Labs
Biologic stability characterization traditionally requires juggling disjointed data from multiple instruments. UNcle reduces these complications and conserves samples by combining fluorescence, SLS, and DLS detection modes in one instrument. This enables 11 different protein characterization applications, and allows for sizing, polydispersity, thermal melting, and aggregation data to be obtained at the same time from the same sample. We will demonstrate how UNcle can thoroughly characterize more biologics and formulations quickly and easily.
3:15 Networking Refreshment Break

3:45 Km and Vmax, and O. Oh, My! Adventures in the Development and Qualification of Methods for Enzymes and Oxidized Proteins
Melissa Clague, Ph.D., Principal Research Scientist, Bioprocess Pharmaceutical R&D, Eli Lily and Company
Complex products can require specialized assays. This talk will cover two case studies: the development and validation of a plate-based assay to determine the essential kinetic parameters, Km and Vmax for a therapeutic enzyme, and the development and qualification of an LC-MS method for quantitation of oxidation of a specific peptide in an antibody project.

4:15 Development of a Fast, Site-Specific Method for Monitoring Oxidation on a Complex Antibody-Based Fusion Protein
Fabio Camerini, MSc, Associate Researcher, Protein Chemistry, Analytical Method Development, Merck Serono S.p.A.
A fast LC-UV method to monitor oxidation in a site-specificway has been developed on a complex antibody-based fusion protein. After having identified protein’s sites prone to oxidation by characterizing artificially degraded samples, a peptide mapping method has been developed to monitor a specific Met residue. Mass spectrometry characterization confirmed the method specificity, while method robustness was studied by applying a DoE. The method developed has been successfully applied to support the process development and the selection of the final formulation.

4:45 Roundtable Breakout Session
Join your peers and colleagues for interactive roundtable discussions.

5:45 End of Day / Short Course Registration

6:00-8:30 pm Dinner Short Courses*
*Separate Registration Required. See Page 2 for details

6:30 Networking Refreshment Break

7:30 Dinner Short Courses*

8:00 am Morning Coffee

8:30 Chairperson’s Opening Remarks
Steven Walfish, MS, MBA, Principal Science & Standards Liaison, Global Science and Standards Division, United States Pharmacopeia

TECHNIQUES AND APPROACHES FOR METHOD DEVELOPMENT AND QUALIFICATION

8:40 Use of Design of Experiment (DoE) for Optimization of ADC Potency Assays
Kenneth R. Miller, Ph.D., Senior Scientist, Bioassay Development, Analytical Sciences Department, Biopharmaceutical Development, MedImmune
The first stage in an analytical procedure lifecycle approach is procedure design. A design of experiment (DoE) study is a useful tool during procedure design to evaluate multiple variables systematically. One can perform a DOE study to identify optimal assay conditions allowing for the establishment of robust fit-for-purpose potency assays. In this talk, examples of DOE studies performed during the development of ADC potency assays will be presented.

9:10 Statistically Based Methods for Determining Target Measurement Uncertainty (TMU)
Steven Walfish, MS, MBA, Principal Science & Standards Liaison, Global Science and Standards Division, United States Pharmacopeia
The analytical target profile states the acceptable error in the measurement. In other words, it states the allowable target measurement uncertainty (tmu) associated with the reportable value of an analytical method. This talk will focus on the statistical methods used to determine the fraction of future results that could be expected to be outside a prespecified specification at a given level of confidence.

9:40 Overcome Soluble Target Interference in Developing Immunogenicity Assays
Dong Geng, Ph.D., Principal Scientist, Biologics and Vaccine Bioanalytics, Merck
Soluble target posts special challenge for immunogenicity assay. Soluble target may result in elevated false positive, sometimes false negatives if ADA assay is not developed properly. This applies to both ADA binding and Nab assay. The presentation will propose couples of approach on how to manage the target interference with case studies.

10:10 PerkinElmer Solutions to Facilitate the Development, Qualification & Validation of Biotherapeutics
Roger Bosse, Ph.D., Sales Development Team Lead, North-America, Life Sciences & Technology, PerkinElmer
Accurate and reproducible technologies are essential for the development of robust methods that can be validated and easily transferred within the biotherapeutics workflow. We will present some of our capabilities that are applicable to the different stages of Biotherapeutics drug development ranging from pre-clinical to commercial manufacturing. Representative applications and distinct customer cases will be reviewed.

11:20 Phase Appropriate Approach for Bioassay Development, Validation, and New Technology Implementation in Quality Control Laboratories
Elena Belitsky, Ph.D., Director, QC Clinical Operations, Biogen
There are different requirements for Bioassays developed for early stage clinical programs compared to late stage programs. Phase appropriate approach for method development, qualification and validation for Bioassay will be presented. Introduction of new technology in GMP environment (Quality Control) is a challenging task requiring special considerations. Major points to consider before implementing a new technology based method in QC will be discussed.

11:50 Platform Approach for Method Development and Qualification during Early Clinical Phases
Claire Davies, Ph.D., Head, Bioanalytics, Sanofi
In early drug development it is important to reduce costs and move quickly from candidate selection to the clinic. Approaches to streamline method development and qualification using risk based and QbD approaches will be presented.

12:20 pm Close of Method Development, Qualification & Validation
HARNESSING TECHNOLOGIES TO SPEED INNOVATION

EMERGING TECHNOLOGIES AND NEW STANDARDS FOR STRUCTURE-FUNCTION ELUCIDATION

1:50 Featured Presentation: Cutting-Edge LC and CE-MS Methods for mAbs, Biosimilars, ADCs and Bispecific Antibodies

Alain Beck, Ph.D., Senior Director, Analytical Chemistry, NBEs, Center d’Immunology Pierre Fabre

The development and optimization of mAbs and related products rely on improving their analytical and bioanalytical characterization by assessing multiple critical quality attributes (CQAs). Case studies on progresses of multi-level (top, middle, bottom, SMDs) state-of-the-art MS methods will be presented. These methods include native MS, Ion Mobility-MS, CE-MS, 2D-LC-MS, Extended Bottom Up and Top Down Sequencing combined with chromatographic and electrophoretic techniques.

2:20 Solving Protein Development Challenges with Hydrogen Exchange Mass Spectrometry

David D. Weis, Ph.D., Associate Professor, Chemistry and Pharmaceutical Chemistry, University of Kansas

Hydrogen exchange mass spectrometry (HX-MS) is gaining acceptance for its ability to monitor higher order structure in proteins, in particular in antibody-based therapeutics. This talk will highlight two areas of recent work focused on solving challenging in development. First, work aimed at developing a molecular level understanding of how protein-exciptent interactions alter physical stability will be presented. Second, the use of HX-MS to map sites of reversible self-association in IgG1 mAbs at protein concentrations > 50 mg/mL will be presented.

2:50 Integrated Methods for Fingerprint Analysis of Recombinant Proteins

Darryl Davies, Ph.D., Associate Director, Analytical Development, Janssen R&D

3:20 Automated Data Processing for Quality Monitoring of Biotherapeutics by Multi-Attribute Methods (MAMs)

Joe Shambaugh, Ph.D., Senior Scientific Account Manager, Expressionist, Genedata

MS-based methodologies enable measurement at the molecular level of many quality attributes of biomolecules. Applying these multi-attribute methods (MAMs) can increase product quality while reducing development and manufacturing costs. We present an implementation of MAMs using Genedata Expressionist®, the software platform for processing, analysis, and management of MS data. Fully automated workflows are employed as part of a bioprocess control strategy to measure critical quality attributes, while searching for impurities and checking the system stability.

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

JOINT SESSION: MULTI-ATTRIBUTE METHODS FOR PRODUCT AND PROCESS CHARACTERIZATION

4:30 Leveraging the Multi-Attribute Method (MAM) to Improve Biotherapeutic Characterization

Richard Rogers, Ph.D., Scientist 4, Just Biotherapeutics

Characterization of complex biotherapeutics using highly resolving mass spectrometry has resulted in a better understanding of the post-translational modifications that are crucial for safety and efficacy. These modifications are used to guide the manufacturing process and the release strategy for biotherapeutics. We have developed and implemented a mass spectrometry based multi-attribute method (MAM) that monitors known modifications but also has the ability to identify new modifications on the biotherapeutics.

For more information on MAM join our MAM Short Course on Monday March 20

5:00 Considerations for Optimization of Multi-Attribute Peptide Mapping Protocols

Trina Formolo, Ph.D., Research Chemist, Bioanalytical Sciences Division, Material Measurement Laboratory, National Institute of Standards and Technology (NIST)

While a powerful, streamlined data analysis workflow is important in building a successful multi-attribute method (MAM) platform, the platform must also incorporate optimized sample preparation and analysis protocols. The generation of reliable, meaningful results from any MAM platform begins with quality sample preparation and analysis. This includes developing robust, reproducible tryptic digestion protocols and optimizing chromatographic separation methods to facilitate the detection and quantification of critical quality attributes (CQA).

5:30 Subunit Analysis Leads to Simultaneous Measurement of Multiple Attributes of Monoclonal Antibodies

Linda Yi, Ph.D., Scientist II, Analytical Development, Biogen

Heterogeneity of therapeutic antibody products as a result of enzymatic/chemical modifications during bioprocessing and storage is well-documented. Routine monitoring of the modifications is essential to ensure product quality. IdeS, an endopeptidase, cleaves antibody at heavy chains below the hinge region, producing F(ab’)2 and Fc/2 fragments. LC-MS analyses of the IdeS digestS, with or without further reduction, enables simultaneous characterization of domain-specific modifications and probing higher order interactions such as high molecular weight species.

6:00 Welcome Reception in the Exhibit Hall with Poster Viewing

7:00 End of Day

WEDNESDAY, MARCH 22, 2017

8:00 am Morning Coffee

8:30 Chairperson’s Opening Remarks

Alain Beck, Ph.D., Senior Director, Analytical Chemistry, NBEs, Center d’Immunology Pierre Fabre
DEVELOPABILITY ASSESSMENT
8:40 Developability Assessment and Epitope Characterization at the Early Stage of Therapeutic Antibody Discovery
Sam Wu, Ph.D., Principal Scientist, Biologics Research, Janssen R&D
Biophysical and chemical properties are critical factors that can dictate success or failure in the development of therapeutic antibodies. Early quality control and risk assessment help prevent failure in later stages of antibody development. An early-stage developability workflow and high-throughput epitope selection were designed to set stage gate for molecules progressing to late-stage development. The collective information identify the best candidates to move forward through the development process.

9:10 Developability Assessment of Bispecific Antibodies: Analytical Platform and Stability Studies
Sagit Hindi-Jacobs, Ph.D., Principal Scientist, BioAnalytical Research, Eli Lilly and Company
The development of bispecific antibodies can present unique challenges for manufacturing and characterization. Attributes such as product purity, biophysical properties, stability and solubility are critical for the development of bispecific antibodies and need to be investigated at early stage of development. This presentation will discuss the analytical platform and stability studies that enable efficient developability assessment of IgG-like bi-specific antibodies.

10:40 Roundtable Breakout Session
Join your peers and colleagues for interactive roundtable discussions.

Topic: Rational Selection of Assays for Early Stage Characterization
Moderator: Liangyi Zhang, Ph.D., Senior Scientist, Analytical Development, AbbVie
• Assays for discovery, candidate selection and developability assessment
• Throughput vs quality of analytical assays
• Adoption of novel technologies
• Bridging assays between Discovery and Development

CHARACTERIZATION IN EARLY DEVELOPMENT
11:20 Selection of High Quality Biotherapeutics: A Stage Approach to Biophysical Assessment of Early Leads
Amy King, Senior Scientist, Biomedicine Design, Pfizer
A two-staged approach is used to identify lead molecules with superior biophysical properties and qualities that support ease of developability. Stage I assessment is designed to triage and de-select proteins that may have high thermal stability, high aggregation propensity, or a tendency toward self-association. Stage II assessment is performed on the prioritized leads to explore behavior at high concentration, such as solubility, viscosity, and colloidal stability. Another key selection criterion is performance in the forced degradation assay to assess sequence hot spot liabilities.

12:20 pm Luncheon Presentation:
Sponsored by FUJIFILM

Exposing Character of a Protein with Advanced Analytics
Gayathri Vasudevan, Ph.D., Principal Scientist Group Leader, Analytical and Formulations Development, FUJIFILM Diosynth Biotechnologies

The emergence of more complex biotherapeutics has diminished the use of platformed analytics and increased the demand for more advanced analytics and individualized characterization steps for development of these products. How we evaluate the “character of a protein” along the process development trajectory is a critical component in developing robust processes and overcoming challenges associated with these new, unique and difficult molecules.

MONITORING OF STABILITY FOR FORMULATION DEVELOPMENT
2:00 Optimizing Protein Stability through Integration of Cutting-Edge and Rapid Analytical Tools with Rational, Molecule-Specific Approach to Process Development
Danny Chou, Ph.D., President & Founder, Protein Formulation and Characterization, Compass BioSolution, LLC
We are at the dawn of a new era with the emergence of new analytical tools that can enable both prediction and real-time monitoring of protein stability. This presentation will illustrate how to properly combine some of these new tools with tried and true strategies that consider the key factors that impact physical stability of proteins in solution. Emphasis will be placed on high-throughput, low sample requirement strategies that are useful for industrial application.

2:30 ExpiQuantification and Stability Monitoring Are Critical for the Formulation Development of Biologics
Joseph Liu, Ph.D., Principal Research Scientist, Formulation, Eli Lilly and Company
The quantity and stability of excipients have direct impact on formulations. They may affect stability and efficacy of API as well as stability and effectiveness of other excipients. Here, we display a method for monitoring the quantity and stability of a commonly used expiuent in biologics formulation. Other excipients existing in the same formulation also changed the stability of this critical expiuent. Real case studies and their outcomes are presented.

PARTICULATE QUANTIFICATION AND CHARACTERIZATION
4:10 Regulatory Perspectives in New Analytical Methods for Protein Aggregates Quantification and Characterization
Ewa Marszal, Ph.D., CMC Reviewer, Hematology Research and Review, Center for Biologics Evaluation and Research, US FDA
Characterization of the size, structural and chemical heterogeneity of protein aggregates in biotherapeutics requires the use of multiple analytical methods. To facilitate and enhance aggregates characterization new methods are being developed, current methods are being improved and established methods are being adapted from other fields. Understanding the advantages and limitations of these techniques by biotherapeutics manufacturers, analytical service labs and regulators
is critical to the improvement of the product quality control and determining the links between the presence of protein aggregates and product safety.

Middle-down subunit analysis of mAb using IdeS digestion has gained popularity for analyzing post-translation modifications, such as glycosylation. Here it was also demonstrated to be valuable for analyzing mAb aggregation. A reducing SEC-MS method with the use of mass spectrometry-compatible running buffer was developed to study highly-aggregated samples of a human IgG1 mAb, and the subunits involved in aggregation were confidently identified.

5:10 Investigation of IgG Monoclonal Antibody Aggregation by HDX, Cross-Linking, and Biophysical Tools Joomi Ahn, Ph.D., Scientist II, Analytical Sciences, MedImmune
Aggregation in recombinant human monoclonal antibodies is one of the major concerns for the biopharmaceutical industry and regulators. In this study, we utilized various higher order structural analytics such as hydrogen deuterium exchange mass spectrometry, cross-linking mass spectrometry, and conventional biophysical tools to investigate the structural differences and the interaction of IgG aggregated forms.

5:40 Close of Advances in Characterization Methods & Approaches Tuesday, March 21, 2017
12:20 pm Registration
1:45 Chairperson’s Opening Remarks Alistair Kippen, Ph.D., Vice President, Biologics Development, Ipsen

BUILDING QUALITY INTO BIOLOGICS

1:50 Featured Presentation: Predictions of Glycosylation Profiles from Cell Engineering and Bioprocess Control Michael Butler, Ph.D., CSO, National Institute for Bioprocessing Research & Training (NIBRT)
The glycoform profile of a biopharmaceutical may determine functional properties that affect therapeutic efficacy. For example, common variations of the conserved Fc glycan of a Mab include galactosylation, fucosylation and sialylation.

The observed glycan profile of the final product depends upon the producer cell line, growth media, culture conditions and protein structure. The control of bioprocess parameters is essential to minimize batch to batch variation and obtain predictable glycan profiles. Strategies will also be discussed to produce Mabs with pre-defined glycan structures.

2:20 New Paradigm of Building Quality during Manufacture – Challenges with Biological Products Rajesh K. Gupta, Ph.D., Co-Owner & Principal Consultant, Biologics Quality & Regulatory Consultants, LLC, former Deputy Director and Lab Chief, Division of Biological Standards and Quality Control, CBER, FDA
Historically, quality of biological products has been ensured through testing representative samples. Shift in quality paradigm started with implementation of Good Manufacturing Practice (GMP) regulations with current focus on building quality during manufacture. Inherent variability and complexity of biological products pose challenges in implementing Quality by design (QbD) concept. This presentation discusses ways to build quality during manufacture of biological products.

2:50 Role of Process Analytics in Improving Process Performance Indresh K. Srivastava, Ph.D., Vice President, Process and Analytical Development, Protein Sciences Corp.
The goal of bioprocessing is to reduce process variability, and improve the product quantity and quality in a reproducible, scalable and transferable way. However, bioprocesses are complex and often results in batch-to-batch variability. This presentation outlines Protein Sciences’ process analytics strategy to improve process performance and understanding, and reduce the process variability.

3:20 Sponsored Presentation (Opportunity Available)
3:50 Refreshment Break in the Exhibit Hall with Poster Viewing
quality. IdeS, an endopeptidase, cleaves antibody at heavy chains below the hinge region, producing F(ab')2 and Fc/2 fragments. LC-MS analyses of the IdeS digests, with or without further reduction, enables simultaneous characterization of domain-specific modifications and probing higher order interactions such as high molecular weight species.

6:00 Welcome Reception in the Exhibit Hall with Poster Viewing
7:00 End of Day
**Wednesday, March 22, 2017**

8:00 am Morning Coffee

8:30 Chairperson’s Opening Remarks
Stephan O. Krause, Ph.D., Director, QA Technical Support, AstraZeneca Biologics

**PAT FOR CONTINUOUS PROCESSING**

8:40 PAT Tools – Online Monitoring and MAM for Continuous Bioprocessing
Bhumit A. Patel, Ph.D., Associate Principal Scientist, Bioprocess Development, Merck & Co, Inc.
Continuous processing for biologics is the way to overcome production challenges in addition to generating consistent product quality. Process analytics is key for the characterization of complex biologics such as mAbs while providing proper process control. Some PAT tools include online U/HPLC to monitor CQAs such as aggregation, charge heterogeneity, and concentration. In addition, Multi Attribute peptide mapping method (MAM) provides critical information on product quality at a molecular level.

9:10 The Use of an LC-MS/MS Multi-Attribute Method for Process Characterization
Kristin Krukenberg, Ph.D., Analytical Scientist, Process Development, Shire
Complex biologics provide a unique analytical challenge for characterizing and monitoring multiple CQAs. We developed an LC/MS based approach that provides more detailed information than six “standard” analytical methods reducing analytical testing time and allowing for more comprehensive and timely support of process characterization and development. Using this method, we have gained understanding of the impact of process parameters on product quality.

9:40 Roundtable Breakout Session
Join your peers and colleagues for interactive roundtable discussions.

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

11:20 Process Modelling and Real-Time Control for On-Demand Manufacturing Biopharmaceuticals on Demand
Richard Braatz, Ph.D., Edwin R. Gilliland Professor of Chemical Engineering, Massachusetts Institute of Technology
This presentation describes the construction of process models and their application to the real-time control of biologic drug production in a small-footprint biomanufacturing platform. An opportunity is the use of a “virtual” plant for the dynamic operations of the entire end-to-end biomanufacturing process. The virtual plant can guide the selection of a control strategy for each critical quality attribute (CQA), design of startup and shutdown operations, and control systems design.

11:50 Rapid Characterization and CQA Assessment of In-Process Samples during Commercial Process Development within High-Throughput Analytical Environment
Ryan Swanson, Ph.D., Scientist II, Process Development Analytics, Bristol-Myers Squibb

12:20 pm Sponsored Presentation (Opportunity Available)

12:50 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

1:20 Dessert Break in the Exhibit Hall with Poster Viewing

1:55 Chairperson’s Remarks

**LINKING CQAS TO CPPS**

2:00 Using Quantitative Proteomics to Link Critical Quality Attributes to Critical Process Parameters
Jonathan Bones, Ph.D., Principal Investigator, National Institute for Bioprocessing Research & Training (NIBRT), University College Dublin
Quantitative proteomics is a powerful tool to understand cellular behaviour at the molecular level. Quantitative proteomics of an IgG1 mAb producing CHO cell line was performed following systematic alteration of bioprocess conditions using a limited Plackett-Burman design of experiments approach. In addition to investigating changes in cellular behaviour, complete characterization of the expressed mAb was also performed to investigate the link between product critical quality attributes and alterations in critical process parameters.
2:30 Application of Multivariate Data Analysis for Process Diagnostics and Root Cause Analysis
Ramila Peiris, Ph.D., Manager, Process Modelling and Process Analytical Technology, Sanofi Pasteur
The utilization of Multivariate Data Analysis (MVDA) techniques at Sanofi Pasteur, Toronto site has demonstrated innovative capabilities for improved process understanding, control and diagnostics. Examples from several successful and high impact applications will be presented. These examples cover the application of MVDA techniques in multivariate process control, root cause investigations and process analytical technology (PAT). The areas of application include fermentation, downstream purification and product formulation stages.

3:00 Sponsored Presentation (Opportunity Available)
3:30 Refreshment Break in the Exhibit Hall with Poster Viewing

INTEGRATED CONTROL STRATEGIES
Sherif Badawy, Ph.D., Research Fellow, Drug Product Science and Technology, Bristol-Myers Squibb

4:40 Recent Advances in Two-Dimensional Liquid Chromatography for Deep and Efficient Characterization, Quality and Control of Biopharmaceutical Materials
Dwight Stoll, Ph.D., Associate Professor of Chemistry, Gustavus Adolphus College
Two-dimensional liquid chromatography is being adopted rapidly in the biopharmaceutical application space. Applications cover the range from discovery and research and development to quality assurance and control. I will give an overview of the most important technology developments in this space in the past five years. I will then share our recent results that show where we can take this technology in the near future, including the characterization of biosimilars.

5:10 Risk-Based Continuous Process Verification (CPV) Response Action Conditions
Stephan O. Krause, Ph.D., Director, QA Technical Support, AstraZeneca Biologics
This presentation provides a risk-based data monitoring/trending matrix for CPV. CPV conditions how to set up and react to alert, action, and out-of-acceptance results are justified. Case studies will be provided to focus on the most challenging aspects when setting up and maintaining a high-value and adaptive monitoring system.

5:40 Close of Process Analytics & Characterization

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Comparability & Biosimilarity
Ensuring Regulatory Compliance and Demonstrating Analytical Control

THURSDAY, MARCH 23 — FRIDAY, MARCH 24

7:30 am Registration & Morning Coffee

8:30 Chairperson’s Opening Remarks
Hans-Martin Mueller, Ph.D., Director, Bioprocess Development, Biologics & Vaccines, MSD

REGULATORY REQUIREMENTS FOR COMPARABILITY/BIOSIMILARITY ASSESSMENTS

8:40 Featured Presentation: An FDA Perspective on Demonstrating Analytical Similarity
Marjorie Shapiro, Ph.D., Chief, Laboratory of Molecular and Developmental Immunology, CDER, FDA

This presentation will focus on the FDA’s expectations regarding analytical similarity data that should be submitted during clinical development and with a BLA submission, as well as analytical bridging studies to leverage non-clinical and clinical data using a non-US approved comparator product.

9:20 Application of a Risk-Based Approach and Advanced Analytical Technologies to Support Comparability Assessments
Valerie Liu Tsang, Ph.D., Technical Development Lead, Biogen

This talk will present recent work aimed at exploring the potential of each analytical approach to differentiate between native and stressed ADC samples. An important aspect of antibody-drug conjugate (ADC) characterization is protein higher order structure (HOS) assessment. Multiple analytical approaches were employed to identify HOS changes between native and stressed versions of an ADC. Datasets from each assay were analyzed statistically to determine the potential of each analytical approach to differentiate between native and stressed ADC samples.

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

DEMONSTRATING COMPARABILITY

10:50 Limits of Detection for Altered Structure in Comparability Studies with Hydrogen Exchange Mass Spectrometry
David Weis, Ph.D., Associate Professor, Chemistry and Pharmaceutical Chemistry, University of Kansas

Recently, there has been considerable interest in the use of hydrogen exchange mass spectrometry (HX-MS) as an analytical tool to demonstrate comparability of higher order structure in therapeutic proteins. This talk will present recent work aimed at exploring the limits of this approach. The detection of small changes in higher-order structure in model systems will be presented. In addition, this talk will advance a general methodology for establishing the limits of detection and suitable statistics for establishment of similarity.

11:20 Similar or Not? Innovative Methods for Active Concentration and Similarity Determination of Proteins and Biological Products.
Robert Karlsson, Ph.D., Staff Scientist, GE Healthcare

Critical Quality Attributes (CQA) are particularly important in the assessment of comparability and biosimilars. In this presentation, we will highlight the use of BiacoreTM SPR for performing comparability and biosimilar studies using both kinetic and Calibration Free Concentration Analysis in applications including antibody screening, Fc-receptor binding, characterization of ADCs and the use of protein probes for detection of stress-induced conformational change.

12:20 pm Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:50 Session Break

1:20 Chairperson’s Remarks
David Weis, Ph.D., Associate Professor, Chemistry and Pharmaceutical Chemistry, University of Kansas

COMPARABILITY OF NOVEL PROTEIN PRODUCTS

1:30 Challenges and Regulatory Requirements for Comparability Assessment of Biotech Products
Joana Qing Zhou, Product Quality Team Leader, Division of Biotechnology Review and Research 1 (DBRR 1), OBP, CDER, FDA

With the increasing complexity of biotechnology products, improvements in analytical methods, and accelerated product development, performing appropriate studies and analyses to demonstrate comparability can be challenging. This talk will discuss regulatory requirements for comparability assessments of biotechnology products at different stages of product development and highlight new challenges emerging from modern biotechnology and bioprocessing.

2:00 Biophysical Methods for Higher Order Structure and Comparability Analysis of Antibody-Drug Conjugates
Brianna Cassidy, Ph.D., Scientist I, Analytical & Pharmaceutical Sciences, ImmunoGen

An important aspect of antibody-drug conjugate (ADC) characterization is protein higher order structure (HOS) assessment. Multiple analytical approaches were employed to identify HOS changes between native and stressed versions of an ADC. Datasets from each assay were analyzed statistically to determine the potential of each analytical approach to differentiate between native and stressed ADC samples.

2:30 Roundtable Breakout Session
Join your peers and colleagues for interactive roundtable discussions

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

4:10 Comparative Analysis of Novel Non-Platform Protein Products
Sophia Levitskaya, Ph.D., Scientist, Analytical Biotechnology, MedImmune

Structural characterization and comparability assessment of non-platform proteins are challenging due to limited product and process knowledge, and high molecular complexity. Case study describes comparative analysis of non-platform biotherapeutics based on thorough pCQA evaluation, characterization of a higher order structure, and application of complementary orthogonal techniques.

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5:10 Development of Platform ADCP and ADCC Reporter Bioassays for Assessing Antibody Effector Function
Arturo Orjalo, Jr., Ph.D., Scientist, ADQC-Biological Technologies, Genentech, a Member of the Roche Group
Antibody-dependent cell-mediated phagocytosis (ADCP) and antibody-dependent cell-mediated cytotoxicity (ADCC) are important mechanisms of action of therapeutic antibodies. We have developed reporter-based bioassays for ADCP and ADCC, and the bioassay work flows for these assays are fast and simple and amenable for measuring the potency and stability of antibodies in a quality-controlled setting. These bioassays are mechanism of action (MOA)-based and have the potential for being platform assays.

5:40 End of Day/Short Course Registration

6:00 – 8:30 Dinner Short Courses*
*Separate Registration Required. See Page 2 for details.

FRIDAY, MARCH 24, 2017
8:00 am Morning Coffee

ESTABLISHING BIOSIMILARITY
8:30 Chairperson's Opening Remarks
David Wyle, Ph.D., Principal Scientist, Sterile Process and Analytical Development, Merck Research Labs

8:40 Preparation of a Strong and Convincing Biosimilar File Supported by Sophisticated Analytical Characterization
Hans-Martin Mueller, Ph.D., Director, Bioprocess Development, Biologics & Vaccines, MSD Merck
Demonstrating comparability for a commercial biosimilar product may present the greatest challenge of an analytical scientist's career. This presentation will talk about the preparation of a robust analytical package for US and EU health authorities; in particular, how to be successful with demonstrating comparability through batch testing, extended characterization, stability studies and forced degradation.

9:10 Analytical Biosimilarity of GP2015 (Erelzi™) to US-Licensed Enbrel®
Urs Lohrig, Ph.D., Lab Head, Phys-Chem-Characterisation, Biologics Technical Development and Manufacturing, Sandoz GmbH
In August 2016, the Food and Drug Administration (FDA) approved Sandoz's Erelzi™ as a biosimilar to the reference product Enbrel® (etanercept) in the United States. This talk summarizes the analytical similarity assessment leading to the successful approval of Erelzi™ and exemplifies results as well as analytical challenges faced during the exercise.

9:40 Sponsored Presentation (Opportunity Available)

10:10 Networking Coffee Break

10:40 Application of PTMs for Comparability and Biosimilarity Assessment
Jane Xiao, Ph.D., Director, Biophysical Characterization, Oncobiologics
Post-translational modifications (PTMs) analysis plays a key role for biosimilar development. High resolution mass spectrometer-based multi attribute peptide mapping technology is used in initiating reference product quality assessment, providing quality range for clone selection, process development, and assessing analytical similarity. The presentation will review the PTMs that may be important in order to align critical quality attributes into quality ranges and minimize batch to batch variation.

11:10 Near UV Circular Dichroism as a Tool for Detecting Higher Order Structure Changes in Innovative/Biosimilar Product Development and Process Comparability of Biotherapeutic Products
Christopher Shaw, Scientist I, Manufacturing Sciences and Technology, AstraZeneca
We have characterized a partially-degraded mAb by biochemical (SEC, CE, peptide mapping, etc.), as well as biophysical (NUV CD and DSC), techniques. The results suggest that these biophysical methods are suitable orthogonal approaches for detecting or confirming protein structural modifications. In this study we describe the sensitivity of a Near UV Circular Dichroism method for detecting such modifications. This method is a useful tool for determining similarity during product development or process comparability of biotherapeutic products.

11:40 pm End of Biotherapeutics Analytical Summit

Hotel & Travel Information
Conference Hotel and Venue
Hyatt Regency Bethesda
One Bethesda Metro Center
Bethesda, MD 20814
Phone: 301-657-1234

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Discounted Room Rate:
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Method Development, Qualification & Validation

Advances in Characterization Methods & Approaches

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Comparability & Biosimilarity

Agenda

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