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Sixth Annual

THE BIOPROCESSING SUMMIT

Practical Solutions for Today's Laboratory Challenges

August 18-22, 2014
Renaissance Waterfront Hotel, Boston, MA

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Event-at-a-Glance

	CONFERENCE PROGRAMS: Monday-Tuesday August 18-19	CONFERENCE PROGRAMS: Wednesday-Thursday August 20-21	CONFERENCE PROGRAMS: Thursday-Friday August 21-22
STREAM 1 Cell Culture & Cell Line Development	Optimizing Cell Culture Technology	Bioproduction: Scale, Bioreactors & Disposables	Optimizing Cell Line Development
STREAM 2 Formulation & Downstream Processing	Overcoming Formulation Challenges	High-Concentration Protein Formulations	Advances in Purification Technologies
STREAM 3 Analytical Development & Quality	Rapid Methods to Assess Quality & Stability of Biologics	Early Analytical Development for Biotherapeutics	Higher-Order Protein Structure
STREAM 4 Development of Next-Generation Biologics	CMC Strategies for Antibody-Drug Conjugates	Process Development for Novel Biotherapeutic Formats	Cell Therapy Bioproduction
Cambridge Healthtech Training SEMINARS*	Introduction to Bioprocessing Global Regulatory Expectations for Analytical Elements of Biotechnology/ Biosimilar Products Pharmaceutical Outsourcing	Introduction to Cell Culture Introduction to Biologics Formulation and Delivery	

SHORT COURSES*:	DINNER SHORT COURSES*:	DINNER SHORT COURSES*:
Monday, August 18 | 9:00-11:30 am	Tuesday, August 19 | 6:00-8:30 pm	Thursday, August 21 | 6:30-9:00 pm

**Separate registration required*

About the Summit

The Bioprocessing Summit

Bringing together the international bioprocessing community

The Bioprocessing Summit brings together international leaders to discuss today's bioprocess issues from cell line selection to bioproduction. The Summit provides practical details in a relaxed, congenial atmosphere that promotes information exchange and networking.

The Bioprocessing Summit continues to grow, and now comprises 12 distinct meetings in one event, including cell culture, purification, bioproduction, quality, formulation, and novel biotherapeutic formats. The Summit also features small-group breakout discussions, networking in the busy exhibit hall, an extensive poster display, and an array of in-depth short courses and training seminars.

This leading bioprocess meeting is hosted in Boston each summer along the lively and cosmopolitan harbor waterfront. Hundreds of bioprocess professionals come together each year at the Summit to share practical solutions for today's laboratory challenges with researchers from around the world.

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Short Courses*

**Separate Registration Required. Please visit the event website for more details.*

MONDAY, AUGUST 18, 2014

9:00-11:30 am Pre-Conference Short Courses

SC 1 Optimizing Media – Achieving Super Soup

To grow mammalian cells, researchers need to provide an optimal *in vitro* environment. The key feature of successful cell growth is the culture medium. 'Achieving Super Soup' requires finesse and know-how in order to combine the right ingredients at the right times under the right conditions to achieve high titers. This workshop will provide a foundation for optimizing cell culture media presented by real-world experts who will also tailor a portion of the course to fit concerns and challenges faced by the workshop participants.

Instructors: Alan G. Ryder, Ph.D., Senior Lecturer, Nanoscale Biophotonics Laboratory, School of Chemistry, National University of Ireland-Galway (NUIG)

Kamal Rashid, Ph.D., Director, Biomanufacturing Education and Training Center, Worcester Polytechnic Institute

Seshu Tummala, Ph.D., Senior Scientist, Manufacturing Sciences and Technology Group, Lonza Biologics, Inc.
Additional Instructors to be Announced

SC 2 QbD Strategies for Formulation Development of Protein Therapeutics

This course offers a forum, discussing how to perform protein drug formulation development to meet Quality by Design expectations from the health authorities. A number of case studies will be presented to demonstrate how to design multivariate experiments, how to obtain dataset and how to analyze data in order to propose formulation of drug substance or drug product. The course will combine "how to" suggestions and real-world examples in an interactive discussion.

Instructors: Steven LaBrenz, Ph.D., Scientific Director, Drug Product Development, Janssen R&D
Kevin Zen, Ph.D., Manager, Biologics Development, Allergan

SC 3 Operational Excellence in Bioprocessing: PAT, QbD, DoE and Continuous Improvement

Ensuring quality in bioprocesses that complies with regulatory requirements and mitigates risk often results in very high bottom-line costs. Adopting best practices early in the development process and customizing these approaches to operational excellence from other highly competitive industries are currently taking place in biopharmaceutical production. This course will provide both an overview of these approaches and how they work, as well as case studies of how these innovations have been applied successfully in bioprocessing and the development of biopharmaceuticals. Appropriate regulatory guidance will also be discussed.

Instructors: Elizabeth Rebeil, Associate Director, Operational Excellence, Shire Pharmaceuticals

James Blackwell, Ph.D., M.B.A., President, The Windshire Group, LLC

Ambarish Singh, Ph.D., Director, Chemistry Manufacturing & Control, Bristol Myers Squibb Co.

SC 4 ADC "Developability": Critical Quality Attributes Inform Formulation and Process Development

ADCs have unique critical quality attributes (CQAs) that are affected by the nature of the component parts: the antibody, the linker and the toxin. The CQAs are also strongly affected by the formulation, the process parameters, and the storage conditions. Effective formulation and process development strategies are based upon a molecular understanding of ADC CQAs: aggregates, charge variants, drug antibody ratio, conjugation site, free drug. Development of these complex molecules requires an array of analytical and biophysical techniques that are used to identify attributes that could have a clinical impact

Instructor: Janet Wolfe, Ph.D., President & CEO, Wolfe Laboratories

TUESDAY, AUGUST 19, 2014

6:00-8:30 pm Dinner Short Courses

SC 5 Extractables & Leachables: Study Design for Disposables and Qualification Consideration

Along with reviewing the history of E&L study designs, this course will also clarify the differences between designing E&L studies for disposable versus primary packaging, and how to use supplier data. We will also look at container closure integrity tests, and discuss E&L test methods development and validation. Finally, we will assess strategies for simplifying and reducing the numbers of E&L studies required, especially with specification changes.

Instructor: Ken Wong, Deputy Director, MTech/AP&T - Extractables & Leachables, Sanofi Pasteur

SC 6 Accelerated Stability Testing of Biologics

This short course will aim to guide the researcher in designing studies for accelerated stability testing of biologics. The course will begin with basic underlying concepts governing protein drug product stability, and focus on design principles for meaning stress and accelerated stability testing of not only the protein of interest, but also of excipients and primary packaging components. Strategies to handle complexities arising from their interactions will also be discussed.

Instructors: Yatin R. Gokarn, Ph.D., Narotam Sekhsaria Distinguished Professor of Chemical Engineering, Institute of Chemical Technology, Mumbai, India

John Iannone, Program Manager and Technical Specialist, Toxikon Corporation

SC 7 Analytical Strategies for Comparability in Bioprocess Development

Bioprocess changes can impact quality attributes of biologics and may affect efficacy and/or safety of the product. During development and throughout the product lifecyle, when process improvements are implemented, it is essential to gather sufficient data to support the conclusion that product safety or efficacy has not been adversely affected. This demonstration exercise requires careful planning of the comparability studies and is based on the background knowledge of protein structure, biological function, and clinical attribute profiles of the product accumulated during development.

Instructor: Christine P. Chan, Ph.D., Principal Scientist/ Technical Lead, Manufacturing Science & Technology, Genzyme, a SANOFI company

THURSDAY, AUGUST 21, 2014

6:30-9:00 pm Dinner Short Courses

SC 8 Biophysical Characterization in Developing Biopharmaceuticals: The Path to Developability, Stability and Comparability

This interactive dinner course will take a closer look at the biophysical toolbox and approaches for monitoring the higher order structure (HOS) of protein drugs.

Instructors: Steven Berkowitz, Ph.D., Consultant; former Senior Principal Scientist, Analytical Development, Biogen Idec

SC 9 ABC: Anything But Chromatography – Precipitation, Crystallization and Flocculation

Increased titer in biopharmaceutical production requires new strategies for economical processing. Precipitation, crystallization and flocculation are a unit operation which overcomes productivity limits of chromatography. General engineering principles, including how to set up a precipitation, crystallization, or flocculation process for purification of recombinant proteins will be shown. Scale-up rules will be explained. Examples will be shown for products produced in mammalian cell culture and E.coli. A strategy on how to implement such processes will be discussed.

Instructor: Alois Jungbaer, Ph.D., Professor, Department of Biotechnology, University of Natural Resources and Life Science Vienna, (BOKU) and Austrian Centre of Industrial Biotechnology

SC 10 Bioprocess Development: Considerations for the Quality and Safety of Materials in Contact with Biologics

This course will discuss in details materials Strategy for bioprocessing, manufacturing and storage of biologics and its impact on overall stability of biotherapeutics. Course will aim to discuss regulatory expectations and analytical strategy for assessing suitability of components, container closure components/primary system. The course will also discuss how the understanding of chemistry of materials such as plastic, rubber, glass and metals and their impact on bioprocess development and overall quality and stability of biologics.

Instructors: Diane Paskiet, Ph.D., Director, Scientific Affairs, West Pharmaceutical Services
Jeffrey Carter, Ph.D., Strategic Projects Leader, GE Healthcare

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Cambridge Healthtech

Training SEMINARS

AUGUST 18-19, 2014

DAY 1 1:00-5:15 PM | DAY 2 8:30 AM - 5:00 PM

TS 1: INTRODUCTION TO BIOPROCESSING

Instructors:

Susan Dana Jones, Ph.D., Vice President and Senior Consultant, BioProcess Technology Consultants, Inc.

Sheila G. Magil, Ph.D., Senior Consultant, BioProcess Technology Consultants, Inc.

CHI's Introduction to Bioprocessing training seminar offers a comprehensive survey of the steps needed to produce today's complex biopharmaceuticals from early development through commercial. The seminar begins with a brief introduction to biologic drugs and the aspects of protein science that drive the intricate progression of analytical and process steps that follows. We then step through the stages of bioprocessing, beginning with the development of cell lines and ending at the packaging of a finished drug product. The seminar also will explore emerging process technologies, facility design considerations and the regulatory and quality standards that govern our industry throughout development. The important roles played by the analytical and formulation in developing and gaining approval for a biopharmaceutical are also examined.

This 1.5-day class is directed to attendees working in any aspect of industry, including scientific, technical, business, marketing or support functions, who would benefit from receiving a detailed overview of this field.

About the Instructors:

Susan Dana Jones is a seasoned biotechnology entrepreneur with experience in product development, outsourcing and strategic planning. Dr. Jones is a subject matter expert in cell line development and characterization for biosimilar, new biopharmaceutical, and vaccine development programs.
She has broad knowledge of regulatory requirements for manufacturing products for human use and has prepared CMC sections of multiple regulatory submissions. She currently serves on the Board of Directors of Gene Solutions, the Scientific Advisory Board of Symphogen, and is a member of the Editorial Advisory Board of BioProcess International.
She received her Ph.D. in Genetics from the University of California, San Francisco.

Sheila Magil has over 20 years of experience in quality and analytical method development for biologics, peptides and small molecules. Her expertise includes quality assurance, protein and peptide biochemistry, and analytical development.
She was formerly Senior Manager of Analytical Development and Quality Control at Biomeasure, Inc., and previously held positions at WaratahPharma, Alkermes, Bion, and HHMI at Massachusetts General Hospital. Dr. Magil has implemented quality systems and has managed external analytical and QC activities for multiple biopharmaceutical products. Dr. Magil holds a Ph.D. in Biochemistry from the University of Minnesota.

TS2: GLOBAL REGULATORY EXPECTATIONS FOR ANALYTICAL ELEMENTS OF BIOTECHNOLOGY/BIOSIMILAR PRODUCTS

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

This 1.5 day class will present the driving concepts that distinguish the regulatory approach to the production and testing of biologically-derived from chemical, small molecule pharmaceutical products. It provides a comprehensive overview of how analytical elements come together in global regulatory dossiers, which can (should!) be used to drive the nature and timing of key CMC studies. It also provides an overview of how regulatory dossier CMC sections in marketing authorizations (BLA/MAA) are linked to analytical expectations in regulatory pre-approval inspections. All attendees will be given a searchable USB drive containing over 200current and draft global regulatory and quality guidance documents associated with the development and commercialization of biotech and biosimilar products. Topics include:

- Why are regulations different for biopharmaceutical products vs. traditional chemical products?
- What are the multiple types of world-wide regulations that detail CMC analytical study requirements for biotechnology/biosimilar products?
- What are the 10 (or 11 if biosimilar) non-negotiable CMC characterization, comparability, release specification and stability data packages required for a biotechnology-based product?
- How can these required CMC analytical and stability studies be staged most efficiently during the product development lifecycle?
- Why do biotech products require orthogonal methods for physiochemical characteristics as well as functional potency assays?
- What are some of the current CMC 'hot buttons' for biotechnology analytical and stability studies that may cause regulatory review problems due to deficiencies in product dossiers?

About the Instructor:

Nadine Ritter obtained her master and doctoral degrees in cell and molecular biology at Rice University (Houston, TX) on evolutionary mechanisms for subcellular translocation of mitochondrial proteins. She was engaged in basic academic research in the field of extracellular matrix proteins and the process of bone mineralization at the University of Texas Health Science Center in Houston for over 10 yrs. She entered the biopharm industry as a protein chemist in analytical R&D at Abbott Laboratories (Abbott Park, IL). She then became the Director of the Analytical Services Division of BioReliance (Rockville, MD), a major contract testing organization. Since 2002, she has been an international consultant, trainer, speaker and writer for biotech and biosimilar products. In 2003, she was one of six industry and two FDA founders of the CaSSS CMC Strategy Forum, which has led to the publication of major industry/regulatory white papers on CMC topics, and is now being held annually in North America, Europe, Asia and Latin America.

TS 3: OPTIMIZING PHARMACEUTICAL OUTSOURCING

Selecting the Right Partner for Your Business and Getting the Most Out of the Relationship

Instructor:
Trevor Deeks, Ph.D., Consultant, Deeks Pharmaceutical Consulting Services LLC

This seminar covers the outsourcing of all activities associated with biological manufacturing, analysis and characterization. It deals with all aspects from the initial steps to identify a suitable outsourcing partner, through to setting up of long-term commercial manufacturing partnerships. It is aimed at both large and small pharmaceutical companies but is particularly relevant to smaller companies that are heavily dependent on reliable, experienced and technically competent third party contractors. The learning styles include formal presentations, group workshop exercises and interactive discussion sessions and it will benefit both technical specialists and project managers. The seminar will include the following outsourcing topics:

- Identification, assessment and selection of third party contractprs based on competency and quality
- Selection based on the needs of the contract giver – finding the right fit and aligning the cultures
- Quality audits and quality agreements – best practices

About the Instructor:

Dr Deeks has 35 years of experience in pharmaceutical manufacturing, process and formulation development, QC and QA experience. He has developed broad technical expertise and has been involved in the commercialization of a number of currently marketed products.
He has held management roles with major pharmaceutical manufacturing and development companies and has also managed pharmaceutical consulting groups providing auditing, validation, GMP consulting, QA and contract Qualified Person (QP) services.
He is a QP registered in the UK under the provisions of the EC Directive. He has audited and assessed more than 50 contract service providers, globally and has worked with CMOs and CTLs for 25+ years.
He recently led a contract manufacturing group for a medium-sized pharmaceutical company for 4 years, identifying, assessing and negotiating with contract manufacturing organizations (CMOs) and contract testing laboratories (CTLs). During this time he developed systems and tools for identification, selection and management of CMOs, CTLs and contract packaging organizations (CPOs).
He has taught several training courses and workshops for PDA, ISPE, PTI and in-house for pharmaceutical companies as well as being an active presenter at PDA, ISPE, AAPS, Pharmaceutical Society and independent conferences.
He has published over 30 papers in peer-reviewed journals and several books and book chapters. Most recently he was lead editor and an author for a new book entitled Pharmaceutical Outsourcing: Quality Management and Project Delivery, now available through PDA Publications.

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Cambridge Healthtech
Training SEMINARS

AUGUST 20-21, 2014
DAY 1 9:00 AM - 5:15 PM
DAY 2 8:30 AM - 12:00 PM

TS 4: INTRODUCTION TO CELL CULTURE

Instructor:
Timothy W. Fawcett, Ph.D., Director, the BioTechnical Institute of Maryland, Inc., and Founder, BioSciConcepts

This 1.5-day Intro to Cell Culture Training Seminar is a lecture based course intended for the beginner who is thinking about culturing animal cells for the first time or for intermediate cell culturists wanting to know more about how animal cell culture works and how to improve their process. Attendees will learn about most of the critical aspects of cell culture from equipment maintenance and media selection to cell growth and cryopreservation. Participants will have ample time to ask specific questions and get worthwhile answers.
Topics to be discussed:

- Introduction to Cell Culture
- Equipment use and decontamination
- Biological safety cabinets and CO2 incubators
- Contamination prevention and types of contamination
- Cell Culture Media I and II
- Cell verification maintenance and storage
- Cell types, microscopy and confluency
- Transfection technology
- Clonal isolation of animal cells
- Primary culture and animal cell attachment and signaling
- Growth curves, growth strategies for growing animal cells in culture

About the Instructor:
Timothy Fawcett has been in the biotechnology business for over 30 years. Trained as a biochemist he has held senior positions in both academics and industry and has been a mentor to many young scientists throughout his career. For the last 13 years Dr. Fawcett has been the Director of the BioTechnical Institute of Maryland (BTI) a non-profit institute located in Baltimore, Maryland. He is also the Founder and Director of BioSciConcepts, a social venture of BTI that provides hands-on training for professional scientists in cell culture, baculovirus based expression, as well as topics such as molecular biology, PCR and real-time PCR. BioSciConcepts is an internationally recognized provider of expertise in cell culture and the biological sciences and has provided consultation services to several small and large biotechnology companies. Dr. Fawcett has a deep knowledge of biotechnology and has experience in most of the technical aspects of the workflow.

TS5: INTRODUCTION TO BIOLOGICS FORMULATION AND DELIVERY

Instructor:
Timothy Kelly, Ph.D., Vice President, Biopharmaceutical Development, KBI Biopharma, Inc.

The course will focus on strategies to plan and execute preformulation and formulation development studies for biologics, which require co-optimization of multiple physical, chemical and conformational stability attributes while operating under accelerated timelines to deliver the drug to the clinic. The course begins with an overview of biophysical and biochemical properties of proteins. A typical development workflow (including statistical analysis and DOE elements) will be outlined to demonstrate the core elements employed during protein formulation. The course concludes with real-world examples from formulation development projects for both liquid and lyophilized products.

- Basics of protein biochemistry, with focus on folding mechanism, stability and structural hierarchy
- Degradation pathways relevant to biologics shelf life
- Biophysical and analytical characterization tools

About the Instructors:
Pooja Arora is a Senior Manufacturing Technical Specialist in the Global Biologics Manufacturing Science and Technology-Drug Product at Genentech. Pooja has more than twelve years of experience in protein biophysical and analytical characterization. Her responsibilities at Genentech include technical transfer of commercial Drug Product manufacturing process to both internal and external manufacturing sites. Pooja has extensive experience in development of robust drug product and manufacturing process for protein therapeutics, including identification of optimum formulation conditions that impart stability to achieve the desired shelf-life, use time stability and selection of primary packaging components. Pooja earned her Ph.D. in Chemistry from Duke University.
Tim Kelly has over 20 years of experience in protein and nucleic acid characterization. In his role at KBI Biopharma, Tim is responsible for analytical development, formulation development, and quality control. Tim's experience includes the analytical development, formulation development, characterization and/or production of more than 200 clinical and commercial protein therapeutics, including monoclonal antibodies, enzymes, cytokines, fusion proteins, PEGylated proteins, protein vaccines, and peptides. Tim has led the successful formulation development of over 95 clinical and commercial biopharmaceutical products, including liquid and lyophilized dosage forms for intravenous and subcutaneous administration, at protein concentrations ranging from 10µg/mL to 200mg/mL. Tim earned his Ph.D. in Molecular Genetics & Biochemistry from Georgia State University.

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10th Annual

Optimizing Cell Culture Technology

Enhancing Knowledge for Growing Cells

STREAM 1
Cell Culture & Cell Line Development

Suggested Short Course*:
Optimizing Media – *Achieving Super Soup*
Monday, August 18, 9:00-11:30 am

**Separate registration required; see page 3 for details*

MONDAY, AUGUST 18

8:00 am Pre-Conference Registration and Morning Coffee

9:00-11:30 Short Course*: Optimizing Media - *Achieving Super Soup*

**Separate registration required; see page 3 for details*

11:30 Main Conference Registration

PROCESS IMPROVEMENT STRATEGIES

1:00 pm Chairperson's Opening Remarks

Lada Laenen, Ph.D., Head, Cell Culture and Microbiology, MSAT, Genzyme, a Sanofi Company

» 1:10 OPENING KEYNOTE PRESENTATION:

The Future of Cell Culture Technology

Bert Frohlich, Ph.D., Director, Bioengineering, Shire Human Genetic Therapies

This talk will begin with a brief overview of factors influencing the direction of cell culture technology and those shaping the biopharmaceutical industry. The overview will serve to tie together many of the subjects covered in this conference. Emphasis will then shift to large-scale production of recombinant proteins and the increasing need for control of product quality and consistency. Emerging technologies, quality-by-design and tools for optimization and achieving improved process understanding will also be touched upon.

1:45 A Statistical Approach to Enhance Productivity in Cell Culture Fed Batch Processes

Hanuman Mallubhotla, Ph.D., Research Director and Head, Biopharmaceutical Development, Syngene International, Ltd.

A Design-of-Experiments (DoE) methodology was developed in deriving optimal basal media, feed media and process parameter settings for a cell culture process. Fifteen basal media and seven feed media were screened; feed rate and temperature conditions were optimized based on statistically observed interaction profiles as well as amino acid profiles. Through optimized feed rate and biphasic-temperature culture conditions, the titer was increased by > 6.0-fold from ~ 0.5g/L in shake flasks to > 3.0 g/L in bioreactors.

2:15 The Application of Systems Biology in Bioprocess Optimization

Len van Zyl, Ph.D., CEO and CSO, ArrayXpress, Inc.

The integration of a Systems Biology approach to optimize and speed-up upstream and downstream bioprocesses is gaining significant traction in the biopharmaceutical industry. Improving our understanding of the cells, the actual bioreactors themselves, provides for a beginning to end development approach to improve product quality and performance. Systems biology as a concept aims to map all conceivable interactions within a system through a set of measurable variables.

2:45 Refreshment Break

OPTIMIZING CELL CULTURE PROCESSES FOR ANTIBODY PRODUCTION

3:15 Antibody Screening in Mammalian Suspension Cells

Michael R. Dyson, Ph.D., Senior Research Associate, Biochemistry, University of Cambridge, and Group Leader, IONTAS, Ltd.

An important step in the process of recombinant antibody selection and optimisation by phage display is the conversion to IgG and Fab format and multi-parallel expression in mammalian suspension cells. This is to both select for clones that can be expressed in high yield and provide antibodies for cell-based functional assays. Methods will be presented for high-throughput antibody expression in HEK293, CHO and stem cells including case studies for the selection of functionally active antibodies.

3:45 Modulation of the Quality Attributes of a Monoclonal Antibody Using Micro-L Scale Fed-Batch Cultures

Martin Jordan, Ph.D., Scientist, Biotech Process Sciences, Merck Serono SA

A high-throughput DoE approach was used to explore the impact of media and feed components on the main quality attributes of a monoclonal antibody. The experiment was performed using a new cultivation system based on shaking 96-deepwell plates. This integrated early cell culture process development approach was found to be particularly fast and resource efficient and the outcome correlated ideally with confirmations performed in larger cell culture volumes such as shake tubes and small-scale bioreactors.

4:15 Small Group Breakout Discussions

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. Then continue the discussion as you head into the lively exhibit hall for information about the latest technologies.

5:15 Discussion Report-Outs

5:30 Grand Opening Reception in the Exhibit Hall with Poster Viewing

7:00 End of Day

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Optimizing Cell Culture Technology

Enhancing Knowledge for Growing Cells

STREAM 1
Cell Culture & Cell Line Development

TUESDAY, AUGUST 19

7:30 am Registration and Morning Coffee

PRODUCTIVITY & QUALITY: RAW MATERIALS

7:55 Chairperson's Remarks

Jörg von Hagen, Ph.D., Director, Global Cell Culture R & D, Merck

8:00 Cell Culture Media Improvements – Considerations from a Powder Perspective

Jörg von Hagen, Ph.D., Director, Global Cell Culture R&D, Merck

To improve the batch-to-batch consistency of dry powder cell culture media, and narrow the variations arising from chemically defined media, different strategies will be presented to control impurities in complete formulations and single ingredients that are important to understand to control cQA of biopharmaceuticals and allow the reproducible regulation of the bioprocess by simplification of, e.g, feed strategies and simpler powder handling. We will present the correlation of the media dissolution coefficient [dc] and the impact on powder solubility and homogeneity as end points depending on the formulation as a result of the concentrations of hygroscopic molecules.

8:30 An Inflatable Chamber for Cell Culture under Hypoxia

Hua Zhong, M.D., Ph.D., FCAP, Assistant Professor, Pathology and Lab Medicine, Rutgers Cancer Institute of New Jersey, Rutgers Robert Wood Johnson Medical School

Tissue hypoxia is a common pathophysiological process. Since the 1990s, numerous studies have focused on investigating cellular adaptation to experimental hypoxia. An inflatable chamber was created for cell culture under hypoxic conditions. It yielded reproducible results in experiments detecting hypoxia-induced accumulation of hypoxia-inducible factor 1 a (HIF-1 a) and hypoxia-induced expression of HIF-1-regulated genes. Basic properties and additional utilities of the chamber will be discussed and compared to pre-existing ones.

9:00 New Approach to Release Critical Raw Materials: Risk Versus Testing-Based Approach

Lada Laenen, Ph.D., Head, Cell Culture and Microbiology, MSAT, Genzyme, a Sanofi company

Regulatory guidelines require for testing to be conducted in order to confirm safety and consistency. Conducting raw material analysis by selection of appropriate risk assessment tools and identifying test methods, to successfully meet the challenges of testing, can prevent costly production issues and possible delays. Throughout the case studies, approaches and results will be presented in order to address potential risk, impact and remediation plans when introducing new raw materials. Furthermore, control strategies and managing risks will be discussed.

9:30 POSTER HIGHLIGHT: Impact of Light Exposure on Cell Culture Performance and Product Quality

Jan Ressl, Late Stage Cell Culture Engineer I, Genentech, Inc.

9:45 Coffee Break in the Exhibit Hall with Poster Viewing

CULTURING CHO CELLS

10:30 Predicting Maximal Viable Cell Density and Cell Sustainability in CHO Fed-Batch Cultures

Yung-shyeng Tsao, Ph.D., Senior Principal Scientist, BioProcess Technology and Expression, Biologics Bioprocess Development, Merck & Co.

The metabolic profiles of 14 CHO-DXB11 clones in fed-batches were studied. During the exponential growth phase their total cell density were found to be linearly proportional to their respective combined glutamine and glutamate consumption rate. The CHO clones with higher efficiency in converting glutamine and glutamate into cell mass were found to reach higher maximal total cell density as well as higher integral of viable cell concentration (IVCC) in fed-batches. This principle may be useful for clone selection.

11:00 Towards Metabolic Engineering of Mammalian Cells using ^{13}C-Metabolic Flux Analysis

Woo Suk Ahn, Ph.D., Research Associate, Bioinformatics and Metabolic Engineering, Massachusetts Institute of Technology (MIT)

Metabolic engineering of mammalian cells can be performed due to the recent development of molecular design tools. However, selection of target genes is still one of hurdles for metabolic engineering. Currently, 13C-Metabolic flux analysis (13C-MFA) draws interests in quantifying intracellular metabolism using stable isotopic tracer and mass spectrometry. This technology enables us to identify bottleneck metabolic genes and evaluate engineered cells.

11:30 Metabolic Flux Analysis of Amino Acid Pathways in CHO Cell Culture

Véronique Chotteau, Ph.D., Researcher, CETEG Cell Technology Group, Industrial Biotechnology, KTH Royal Institute of Technology

The determination of the metabolic fluxes occurring in the cell and in interaction with its environment is key for a better knowledge of the cell metabolism in culture. Models of the metabolic fluxes provide very powerful tools to understand and simulate the cell metabolism in culture, eventually leading to process optimization. We have developed approaches to model the amino acid metabolism based on their extracellular measurement. Our strategy is to obtain a single model that includes different cell states generating a powerful tool for process optimization.

12:00 pm Sponsored Presentations

(Opportunities Available)

12:30 Luncheon Presentation

(Sponsorship Opportunity Available)

1:15 Session Break

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10th Annual

Optimizing Cell Culture Technology

Enhancing Knowledge for Growing Cells

STREAM 1
Cell Culture & Cell Line Development

CULTURING CHO, MAMMALIAN & INSECT CELLS

1:55 Chairperson's Remarks

Michael R. Dyson, Ph.D., Senior Research Associate, Biochemistry, University of Cambridge, and Group Leader, IONTAS, Ltd.

2:00 AMBR™ 48 as a ToolforProcess Development and Characterization for the Manufacture of a Biosimilar in CHO Cells

Matthew Zustiak, Ph.D., Principal Scientist, Cell Culture Development, Gallus Biopharmaceuticals

A QbD approach is effective in the process development for the development of a biosimilar since the exact critical quality attributes are known. A high-throughput method of process development and characterization is desired. We used the Ambr™ 48 system as a scale-down model for process development and as a tool for key process parameter identification and characterization in the upstream process for the manufacture of a biosimilar. The results of this development will be discussed.

2:30 Scalable Transient Transfection for Antibody & Vaccine Production in Multiple CHO, Insect, and Other Mammalian Cells

Sponsored by MaxCyte

James Bradey, Ph.D., Director, Technical Applications, MaxCyte, Inc.

Flow electroporation streamlines biotherapeutic and vaccine development by enabling large-scale transient gene expression directly in the cells of interest including multiple CHO strains, insect cells and other mammalian cell lines. Flow electroporation produces significantly higher yields for a variety of proteins including antibodies, antibody-like molecules, and vaccines, when compared to other transfection methods. Data will be presented demonstrating the versatility, scalability, and multi-gram production capacity of flow electroporation.

3:00 Mammalian Cell Fluid Mechanics and Scale-Up/Scale-Down Considerations

Jeffrey Chalmers, Ph.D., Professor, Chemical and Biomolecular Engineering; Director, Analytical Cytometry Shared Resource, Comprehensive Cancer Center, The Ohio State University

The perception of "shear sensitivity" has historically put an arbitrary upper limit on agitation and aeration in bioreactor operation; however, as cell densities and productivities continue to increase, mass transfer requirements can exceed those imposed by these arbitrary low limits. This presentation will mainly focus on publications from both academia and industry, and some recent experimental data on microcarrier cultures regarding the effect of hydrodynamic forces on industrially relevant animal cells, and on the general observation with respect to scale-up.

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

EMERGING TOOLS TO SUPPORT CELL CULTURE

4:15 Raman Spectroscopy as a PAT Tool

Sofie Goetschalckx, Head, Cell Culture Manufacturing Science Team, MSAT, Cell Culture and Microbiology, Genzyme, a Sanofi Company

To better understand critical quality attributes of manufactured biologics, and apply the FDA's process analytical technology (PAT) initiative, industry increasingly seeks means by which critical process parameters can be monitored and controlled in real-time. Raman spectroscopy can be a very interesting tool as it is useful for PAT and QbD applications and allows for real-time, quick, in situ monitoring and bioprocess control. Data presented outlines the use of Raman spectroscopy in monitoring cell culture performance in recombinant protein production.

4:45 Comprehensive, Quantitative Bioprocess Productivity Monitoring Using Fluorescence EEM Spectroscopy and Chemometrics

Alan G. Ryder, Ph.D., Senior Lecturer, Nanoscale Biophotonics Laboratory, School of Chemistry, National University of Ireland, Galway

Fluorescence excitation-emission matrix (EEM) spectroscopy is used for quantitative predictive analysis of glycoprotein production in a CHO cell fed-batch process. EEM spectra of complex solutions are very sensitive to compositional change and as cultivation progressed, the emission of tyrosine, tryptophan, and the glycoprotein product showed significant differences, and this was used to follow culture progress via chemometrics. A second aspect of the study involved developing quantitative predictive models of process performance based on glycoprotein yield. This methodology opens the possibility of early-stage intervention for poorly performing lots.

5:15 End of Conference

5:15- 6:00 Dinner Short Course Registration

6:00 – 8:30 Dinner Short Course*: Extractables & Leachables: Study Design for Disposable and Qualification Consideration

Separate registration required; see page 3 for details

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4th Annual

Bioproduction: Scale, Bioreactors & Disposables

Making It Work

STREAM 1
Cell Culture & Cell Line Development

Suggested Short Course*:
Extractables & Leachables: Study Design for Disposables and Qualification Consideration
Tuesday, August 19, 6:00-8:30 pm

Separate registration required; see page 3 for details

WEDNESDAY, AUGUST 20

7:00 am Registration and Morning Coffee

BIOPRODUCTION STRATEGIES

8:05 Chairperson's Remarks
Stefan Schmidt, Ph.D., Vice President, DSP, Rentschler Biotechnology

» 8:15 KEYNOTE PRESENTATION
The Future of Biologics Development and Manufacturing
Nuno Fontes, Ph.D., Director, Protein Science, Boehringer Ingelheim, Inc.

With monoclonal antibodies dominating today's biologics pipelines, and cost of goods that represent only a very small fraction of drug prices, biologics development and manufacturing is typically focused on fully leveraging and continuously improving a relatively mature "consensus" industry platform. However, the staggering cost of overall drug development in today's pharma business model, as well as, strong pressures to reduce overall healthcare cost will fuel new models such as Biosimilars, Biobetters and personalized or precision medicines. Flexible and innovative development and manufacturing concepts will support these new models.

9:00 Optimization of a Pilot-Scale Model System
William Brazier, Principal Engineer, Amgen

9:30 Fed-Batch Process for the Production of Recombinant Hemagglutinins, Components of Influenza Vaccine Flublok
Nikolai Khramtsov, Ph.D., Associate Director, Upstream Development, Protein Sciences Corporation

We developed a universal process for the expression and purification of influenza recombinant hemagglutinins (rHA) at different scales without re-developing the process for new rHAs. We have optimized the process to manufacture drug substance in less than two months from cloning the gene to the production of drug substance. The fed-batch process yielded at least a two fold increase for all seasonal and pandemic rHAs. The quality of purified rHAs produced by the fed-batch process is similar to rHA proteins produced in batch process.

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

DISPOSABLES

10:45 DSP Single-Use Technologies to Move to a Fully-Closed Process
Steven Strubbe, DSP Specialist, Merck

Single-use biomanufacturing systems promise to reduce the risk of cross-contamination, make clinical development faster, technology transfer easier with a lower process cost, minimal validation and cleaning issues. Thus future process designs will require downstream device innovation to move open phases to fully closed ones. New technologies, such as precipitation in single-use bags or disposable CEX devices for Mab purification were assessed. Performance results as well as process cost, scale-up considerations and facility designs will be discussed.

11:15 Opportunities and Limits of Disposables in Non-Platform Processes
Stefan Schmidt, Ph.D., Vice President, DSP, Rentschler Biotechnology

Single-use systems are an industry standard in platform processes. But current pipelines contain many novel fusion proteins. These molecules are difficult to manufacture due to low titer, lack of an affinity matrix, or tendency to aggregate. In selected case studies, we demonstrate when it is economically and technically reasonable to rely on single use, when a hybrid model is advantageous, or when conventional approaches are preferable. Advice will be given on successful process design, optimization strategies, and critical manufacturing parameters.

11:45 Innovative Simulation Technologies to Optimize Cell Culture
Sponsored by ANSYS
Marc Horner, Ph.D., Lead Technical Services Engineer, ANSYS, Inc.

Cell culture is a delicate process in which cell growth and occasionally cell damage are influenced by flow conditions. Engineering simulation and CFD are used to investigate the transient flow behavior in bioreactors. ANSYS experts discuss how influential parameters affect the flow pattern and hence the evolution of cell culture. This insight opens the door to simulation based process optimization.

12:00 Cleaning and Compliance: Considerations for Today's Bioprocessing
Sponsored by TOXIKON ADVANCING YOUR INNOVATION
Michael Brady, Ph.D., Director, Microbiology Services, Toxikon Corporation

Bioprocessing equipment requires a validated cleaning procedure for efficient bioproduction, product safety, and regulatory compliance. This brief presentation will review critical process parameters, analytical and sampling methods, as well as acceptance criteria for cleaning processes. Maintenance of a validated state and inspection considerations will be presented.

12:15 pm Luncheon Presentation: Scale-Up Evaluation of Mobius CellReady Disposable Bioreactor Operation from 3L to 50L Scale: Best Practices for a Perfusion Application
Sponsored by EMD MILLIPORE
Michael Cunningham, Ph.D., Senior Applications Scientist, Biomanufacturing Sciences Network, EMD Millipore

The Mobius CellReady bioreactor portfolio provides disposable bioproduction capabilities important for

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STREAM 1
Cell Culture & Cell Line Development

the optimal performance of mammalian cell cultures in suspension. This presentation will review the utilization of EMD Millipore's 3L and 50L CellReady single-use bioreactors for a perfusion-based CHO cell bioproduction application, where hollow fiber connection and operation points to consider will be reviewed. In addition, results of the evaluation of scalability from bench to engineering scale will be presented.

1:30 Session Break

BIOREACTOR OPTIMIZATION

1:55 Chairperson's Remarks
Michael Brady, Ph.D., Director, Microbiology Services, Toxikon Corporation

2:00 Scale-Up by Design: How to Design a Production Scale Bioreactor
Yogesh Waghmare, Ph.D., Process Engineer III, Global Manufacturing Science and Technology, Genzyme, a Sanofi Company
This presentation will describe a methodology of how a production scale bioreactor was re-engineered and re-designed in order to reduce the risk of scaling-up a microcarrier-based mammalian cell culture. The approach taken here involved synergistic use of engineering tools including computational fluid dynamics models, empirical analysis and pilot scale wet testing. Three dimensional printing of the pilot scale reactor and its components was chosen as the method to facilitate meeting tight marketing timelines.

2:30 The Application of Advanced Process Control and Model-Based Strategies for Improved Bioprocess Performance
Jessica Whelan, Ph.D., Director, Life Science, APC Ltd The Applied Process Co
The development of robust, consistent and reliable bioprocess performance can be greatly enhanced through the application of model-based strategies which mirror equivalent process development approaches in other manufacturing industries. The integration of such models into process control strategies can further enhance process optimization performance. In this talk, we will present the experimental and theoretical framework for such strategies. In addition, we will discuss some results from specific studies with cell culture processes in PAT-enabled pilot-scale bioreactor batches.

3:00 Using Lactate Dehydrogenase Measurements to Quantify, Understand and Predict Cell Growth in a High-Density Perfusion Bioreactor
Cheng Cheng, Process Engineer, Late Stage Cell Culture Development, Genzyme, a Sanofi company
We developed a model for lactate dehydrogenase (LDH) release kinetics that uses intracellular and extracellular LDH concentration measurements to estimate cell lysis rates as well as intrinsic growth and death rates for high-density CHO cell culture in long-duration perfusion bioreactors. Using this model, we demonstrate that intrinsic cell growth rate remains stable throughout a 60-day bioreactor run despite differences in cell culture performance. We also show that our model for cell death and growth is a useful tool for appropriately calculating generation number across different bioreactor scales.

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

SCALE-UP / SCALE-DOWN

4:15 Case Studies for Utilization of Conventional and CFD Approaches for Successful Scale Up and Scale Down of Bioreactor Processes for Monoclonal Antibodies
Michelle LaFond, Director, Bioreactor Scale-Up and Development, Regeneron Pharmaceuticals
Conventional approaches to scale-up of bioreactor process parameters to new facilities have historically been successful, but not all monoclonal antibody processes are created equal. For some programs, these methods can result in suboptimal process performance and require optimization to be performed at manufacturing scale. More recently, use of both conventional and computational fluid dynamic approaches to develop scale-down, pilot-scale models of production bioreactors have resulted in improved process understanding and more successful transfer for late stage processes. The new scale-down models are more predictive of manufacturing and are used to map out impact of scale-up parameters to process performance. Case studies of both approaches will be discussed.

4:45 High-Throughput System for Cell Culture (HTS-CC) Comparability: Generating Data to Guide 2L Small-Scale Experiments
Kristen Douglas, Ph.D., Scientist and Group Leader, Late Stage Cell Culture, Genentech, A Member of the Roche Group

5:15 Networking Reception in the Exhibit Hall with Poster Viewing

Sponsored by
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6:30 End of Day

THURSDAY, AUGUST 21

8:00 am Registration and Morning Coffee

PROCESS DEVELOPMENT

8:25 Chairperson's Remarks
Jessica Whelan, Ph.D., Director, Life Science, APC Ltd The Applied Process Co

8:30 Process Development Strategies to Enable Robust and Scalable Downstream Manufacturing Processes
Mi Jin, Ph.D., Group Leader, Biologics Process Development, Bristol-Myers Squibb
Monoclonal antibodies (mAbs) and Fc Fusion proteins constitute a major portion of the biopharmaceutical pipeline. Although the framework sequences and structural similarity among this class of molecules enable a platform approach to process development, product specific physicochemical properties can still pose significant challenges for process design, scale up and manufacturing process control. In this presentation, we will use several case studies to show some common challenges in chromatography, high concentration UF/DF and VF process design, and demonstrate the use of combined experimental and model based approaches to identify and mitigate potential issues early during development to deliver

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robust and scalable manufacturing processes.

9:00 Scale-Up Effects on Process Performance and Product Quality

Kishan Rao, MS, Senior Manager, Technical Services, Alexion Pharmaceuticals

Great care must be taken when committing to in-process limits or product quality specifications, particularly when there is limited full-scale process data to set those limits. Often, the clinical experience with a product quality range is what drives the product specification limits. If ranges are set prematurely or set overly narrow, inherent process variability or assay variability can cause the in process limits to be missed, the critical quality attribute to have a failure which ultimately could lead to lot rejection.

9:30 Fast and Easy Generic Anti-CHO HCP Analysis, 96-Samples Assay-To-Data in 65min.

Sponsored by PALL Life Sciences / forteBIO A Division of Pall Life Sciences

Darick Dayne, Ph.D., Senior Product Manager, ForteBio, A Division of Pall Life Sciences

Pall ForteBio has teamed up with Cygnus Technologies to jointly develop an Anti-CHO HCP detection kit. While ForteBio Octet systems are the industry standard in easy and rapid high throughput analysis, Cygnus HCP ELISA kits are known for their broad HCP recognition and sensitivity. The new ForteBio-Cygnus Anti-CHO HCP kit will embody the best of both worlds. Users will achieve unparalleled time-to-results, streamlined and automated* workflow, enhanced dynamic range, and excellent precision and assay robustness.

* Complete hands-off automated workflow achieved with the Octet HTX system

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

ENSURING QUALITY

10:45 Proton Transfer Reaction Mass Spectrometry - A Non-Invasive Approach for Advanced Bioprocess Monitoring

Gerald Striedner, Ph.D., Assistant Professor, Biotechnology, University of Natural Resources and Life Sciences, Vienna

Limited real-time access to physiology relevant process variables is the major obstacle on the way to process understanding and rational process design. Proton transfer reaction mass spectrometry employed for real time measurement of volatile compounds in the offgas stream of bioreactors provides direct access to such meaningful information. Beside this the major advantage of this non-invasive real time monitoring system is that it can be implemented as additional monitoring tool even in already existing GMP production processes without interfering regulatory requirements.

11:15 Evaluation of Monochromatic UV for Viral Inactivation of Mammalian Cell Culture Media

LiYing Yang, Ph.D., Scientist II, Manufacturing Sciences & Technology, MedImmune, Inc., AstraZeneca Supply Biologics

Commercial scale facilities used in the manufacture of biologics using mammalian cell culture can be susceptible to undesirable adventitious agent contamination due to a number of factors including the complexity of the process, equipment, raw materials, and intrinsic property of the cell substrate. The biopharmaceutical industry has taken multipronged approaches to address the risk of viral contamination via testing of adventitious viruses, stringent raw material controls and sourcing, introduction of viral barrier technology in upstream operation, and performing viral clearance procedures in downstream processing activities. In this case study, novel monochromatic UV-B technology is evaluated for its viral inactivating capability of cell culture media, which can pose the highest viral contamination risks to a biologics manufacturing facility due to their complexity and varied composition/ origin. Analytical testing and cell culture use studies were conducted to determine the effect of UV-B treatment on cell culture media and its feasibility for use in biologics manufacture. Preliminary viral inactivation results following UV-B treatment will be presented and discussed.

11:45 Unique Mixing with Minimal Shear in Biobags

Henry Bungay, Ph.D., Emeritus Professor, H.P. Isermann Department of Chemical Engineering, Rensselaer Polytechnic Institute

In a machine that agitates up to sixteen transparent disposable biobags by alternate squeezing and release, unexpected eddies are observed when the front and back walls of the biobag are fastened together in favored locations. Restraining arms with lights and photodiodes send continuous turbidity data to a computer. Mixing determined by signals from the computer can be set visually for very low-shear for tissue culture or for turbulence for molds or bacteria.

12:15 pm Innovative Simulation Technologies for Bioreactor and Process Equipment Design

Sponsored by ANSYS

Marc Horner, Ph.D., Lead Technical Services Engineer, ANSYS, Inc.

ANSYS experts will present simulation solutions for bioreactor and process equipment design. ANSYS simulation can offer insight into chemical reactions, mixing, and multiphase flows commonly found in bioreactors. Engineering simulation also predicts temperature, oxygen and species distribution as a function of the operating conditions in pilot or production reactor designs.

12:30 Luncheon Presentation *(Sponsorship Opportunity Available)*

1:15 End of Conference

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6th Annual

Optimizing Cell Line Development

Enhancing Expression

STREAM 1
Cell Culture & Cell Line Development

Suggested Short Course*

Bioprocess Development: Considerations for the Quality and Safety of Materials in Contact with Biologics

Thursday, August 21, 6:30-9:00 pm

Separate registration required; see page 3 for details

THURSDAY, AUGUST 21

CHO

1:55 pm Chairperson's Remarks

Jesús Zurdo, Ph.D., Head, Innovation, Biopharma Development, Lonza Biologics plc

» 2:00 KEYNOTE PRESENTATION

Moving Beyond the Off-the-Shelf CHO Host to New Improved Expression Hosts

Scott Estes, Ph.D., Director, Cell Culture Development, Biogen Idec, Inc.

CHO does not have a dedicated secretory phenotype and may be ill-equipped to handle the elevated secretory load incurred during the production of biologics. To facilitate a rational selection of candidate targets, we mined published genome wide screens to identify key regulators of secretion. These targets were overexpressed in CHO cells and the resulting engineered hosts studied to determine their ability to express mAbs. Of the fourteen genes investigated, we identified one, a small GTP-binding protein, which significantly improved productivity.

2:45 Evolving to a Rational Bioprocess Model: Applying Lessons from Global Metabolomics of a CHO Process at Lab and Manufacturing Scale

Amanda Lanza, Ph.D., Scientist, Bristol-Myers Squibb Co.

Traditional Bioprocess development is empirical, requiring a large number of experiments for each cell line and process. The result is both time-consuming and labor intensive. Furthermore, a small number of extracellular metrics are used almost exclusively to make key decisions. Alternatively, an ideal approach would be rationally driven, combining extracellular and systems-level intracellular data to guide Bioprocess development. Here we discuss the application of global, unbiased metabolomics on a CHO cell process at both lab and manufacturing scale, and how these findings can be used to refine the development approach. Finally, we discuss how metabolomics profiles and phenotypes observed at the process level can be used to guide future cell line development.

3:15 Optimization of the CHEF1 CHO Expression Platform

Howard Clarke, Ph.D., Director, Upstream Process Development, CMC Biologics

The Chinese Hamster Elongation Factor 1α (CHEF1) platform is designed for the manufacture of recombinant therapeutic proteins in stable CHO cells using chemically defined media. CHEF1 expression has been shown to improve yield over CMV-controlled plasmids in CHO cells and is associated with growth, such that titer increases with volumetric productivity. Recent integration of CMV regulatory domains into the CHEF1 plasmid has led to increased productivity in the later-stage process, increasing production duration and overall yield.

3:45 GPEX™ Cell Line Engineering Case Studies using Multiple Mammalian Cell Lines

Sponsored by Catalent

Andrew Sandford, Vice President, Global Business Development, Biologics, Catalent Pharma Solutions

Through case study examples, attendees will gain an understanding of how GPEX Cell Line Engineering was incorporated into several cell line expression/product development projects. The presentation will discuss the challenges of the overall projects, procedures completed, analysis of data, insights gained, and final conclusions that demonstrate how GPEx® technology was used to generate mammalian cells with high yields and stability, which will help speed the drug to clinic.

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

4:15 CHippO: Manipulation of the Hippo Signaling Pathway in CHO to Produce a Superior Host for Recombinant Protein Expression

John Follit, Ph.D., Scientist I, Cell Line Technology, Biogen Idec, Inc.

The Hippo signaling pathway controls cell proliferation and organ size by activating Yes-associated protein 1 (Yap1). We hypothesized that altering the Hippo pathway may result in an engineered host cell with an improved bioprocessing phenotype. To this end, we created Yap1 overexpressing CHO cells (CHippO) and auditioned the new host with model monoclonal antibodies. CHippO cells exhibited significant boosts in mAb expression with top clones from the engineering CHIPPO host achieving titers up to three times higher than clones arising from an unmodified host.

4:45 Applicability of Readily Grown Mice Cell Lines in Culture for Melanoma Research

Molly Jenkins, Ph.D., Research Fellow, Microbiology and Immunology, Norris Cotton Cancer Center, Geisel School of Medicine, Dartmouth College

Transgenic mouse models allow the study of melanoma *in vivo*, however *in vitro* models are necessary to better understand the molecular mechanisms underlying disease progression and therapy resistance. We have established melanoma cell lines (Dartmouth Murine Mutant Malignant Melanoma; D4M cells) from a conditional mouse model of metastatic melanoma. Here, we report the characterization of these lines, and demonstrate their unique ability to correlate *in vitro* studies on molecular mechanisms of melanoma with *in vivo* investigations on pathology and immunology.

5:15 End of Day

5:45-6:30 Dinner Short Course Registration

6:30-9:00 Bioprocess Development: Considerations for the Quality and Safety of Materials in Contact with Biologics *

Separate registration required; see page 3 for details

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Optimizing Cell Line Development

Enhancing Expression

STREAM 1
Cell Culture & Cell Line Development

FRIDAY, AUGUST 22

8:00 am Registration and Morning Coffee

CELL LINE DEVELOPMENT

8:25 Chairperson's Remarks

Howard Clarke, Ph.D., Director, Upstream Process Development, CMC Biologics

» 8:30 FEATURED PRESENTATION

Cell Line Development Approaches for Speed, Titer and Product Quality

Till Wenger, Ph.D., Associate Director, Cell Biology & Cell Culture II, Process Sciences, Boehringer Ingelheim Pharma

In developing NBEs, speed, titer and an excellent product quality is key. For biosimilars, the essential target is matching the originator product quality. Here, we show how the use of a platform based on well characterized cell lines and thorough process understanding can be used to achieve fast and reliable development of high-titer cell lines, how cell line development can be accelerated, and how specific host cells and processes parameters can be used to influence product quality attributes.

9:00 Antibody Membrane Switch (AMS) Technology for Facile Cell Line Development

Bo Yu, Ph.D., Co-Founder and CSO, Larix Bioscience, LLC

Antibody Membrane Switch (AMS) technology is the most effective and time efficient technology available today for the isolation of production cell lines. AMS technology utilizes a unique switch mechanism of alternative splicing and site-specific DNA recombinase to turn cells from expressing membrane-anchored antibodies into production cells secreting the antibody. This enables screening of hundreds of millions of cells per day by FACS, eliminating the requirement for gene amplification. Utilizing AMS technology can reduce cell line screening time from 6-8 months to 2-3 months.

9:30 Innovative Cell Line Development for the Expression of Glenmark's Novel Bispecific BEAT Format

Pierre Moretti, Ph.D., Staff Scientist and Head, Cell Line Development, Glenmark Pharmaceuticals

Glenmark's BEAT bispecific antibody format is based on engineered IgG scaffolds and maintains key antibody properties such as thermostability, low immunogenicity and pharmacokinetics. Production and purification are achieved using established platform technologies. This presentation will focus on the cell line development. Innovative solutions were found in order to rapidly generate and select high producing, stable cell lines and to drive the optimal pairing of heterologous heavy and light chains while minimizing unwanted side products.

10:00 Mid-Morning Snack in the Exhibit Hall with Poster Viewing

EARLY ANALYSIS OF CELL LINES TO PREDICT DEVELOPABILITY

10:45 Early Pre-Process Risk Assessment: Alternatives to One-Size-Fits-All Process Development to Reduce Product Attrition and Streamline Development

Jesús Zurdo, Ph.D., Head, Innovation, Biopharma Development, Lonza Biologics plc

Biomanufacturing processes are still complex, largely unpredictable, and very much linked to the nature of the product to be made. In most cases, uncertainty is managed with extensive screening, testing and analysis, which is tremendously costly and time-consuming. We present some alternative approaches to development that have a greater emphasis in the design and selection of the therapeutic candidate for optimal safety, stability and formulability, combined with faster approaches for early material generation. Potential impact in streamlining clinical development will be discussed.

11:15 High-Throughput Imaging during Cell-Line Development to Increase the Assurance of Clonality

David Shaw, Ph.D., Group Leader, Early Stage Cell Culture, Genentech, Inc.

11:45 Omics Analyses of Antibody Producing Cell Lines to Improve Productivity and Product Quality

Sohye Kang, Ph.D., Senior Scientist, Product Attribute Sciences, Amgen, Inc.

We examined various production cell lines expressing different therapeutic monoclonal antibodies and investigated their intrinsic properties associated with culture performance and phenotypes. 17 different cell lines displaying a wide spectrum of productivity range were chosen and treated with the same media and process conditions to keep the external factors constant. Microarray-based transcriptomics and LC-MS/MS shotgun proteomics technologies were utilized to obtain expression landscape of different cell lines and reveal cellular mechanisms associated with different culture phenotypes, including productivity, proliferation rate and cell size.

12:15 pm Capabilities of Full Bioprocess Control in Micro Bioreactors for Cell Line Development

Sponsored by

Frank Kensy, Ph.D., Managing Director, m2p-labs, Inc.

A new micro bioreactor platform with microfluidic control will be presented. The new BioLector Pro owns a unique microfluidic plane fused on a microplate to realize continuous pH-control and feeding in up to 32 parallel fermentations at 1ml scale. This single-use microfluidic system was designed to perform cell line development already under process conditions.

12:45 Luncheon Presentation

(Sponsorship Opportunity Available)

OPTIMIZING PRODUCTIVITY & YIELD

1:25 Chairperson's Remarks

Frank Kensy, Ph.D., Managing Director, m2p-labs, Inc.

1:30 Optimization of Biologics Yield in Microbial and Mammalian Expression Systems

Ian Fotheringham, Ph.D., President & Co-Founder, Industrial Biotechnology, Ingenza, Ltd.

E. coli-based expression systems can be unsuitable for the production of certain mammalian proteins/enzymes often yielding insoluble, inactive product. We have developed optimized microbial and mammalian cell lines and expression systems for the production of protein biologics that consistently yield active soluble protein. Our systems are free of third party IP encumbrance, enable manufacturing to GMP standards and facilitate straightforward protein purification.

2:00 Improving Yields in a Novel *Drosophila* S2 Expression System

Wian de Jongh, Ph.D., CSO, ExpreS2ion Biotechnologies

ExpreS2ion Biotechnologies is responsible for the process development of two malaria vaccines in

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collaboration with The Jenner Institute, Oxford University and the Centre for Medical Parasitology, Copenhagen University. It is vitally important to reduce cost-of-goods for these vaccine due to the geographic location of endemic areas and the philanthropic funding sources involved in vaccine distribution. ExpreS2ion has therefore focused on improving yields though cell line selection and process improvement strategies, which will be presented in this talk.

2:30 Highly Multiplexed Subcellular RNA Sequencing *in situ*

Jehyuk Lee, M.D., Ph.D., Genetics, Wyss Institute for Biologically Inspired Engineering, Harvard University

We describe fluorescent *in situ* RNA sequencing (FISSEQ), in which stably cross-linked cDNA amplicons are sequenced within a biological sample. Using 30-base reads from >8000 genes *in situ*, we examine RNA expression and localization in primary fibroblasts during wound healing *in vitro*. Our platform enables massively parallel detection of genetic elements, including gene transcripts and molecular barcodes, for studying cellular phenotype, gene regulation, and environment *in situ*.

3:00 Refreshment Break

CELL LINE DEVELOPMENT INNOVATIONS

3:15 A Vector-Free Microfluidic Platform for Intracellular Delivery and Manipulation of Cell Function

Armon Sharei, Ph.D., Research Associate, Chemical Engineering, Massachusetts Institute of Technology (MIT); Co-Founder, SQZ Biotech

Intracellular delivery of macromolecules is a challenge in research and therapeutic applications. Existing vector-based and physical methods have some limitations, including their reliance on exogenous materials or electrical fields. We describe a microfluidic approach to delivery in which cells are mechanically deformed as they pass through a constriction 30-80% smaller than the cell diameter. By enabling the delivery of RNA, DNA, proteins, and nanoparticles, this technique has demonstrated effective manipulation of cell behavior in a range of applications.

3:45 High-Throughput Automation Solutions in Bioprocess Development

Gregory Keil, MS, Senior Scientist, Merck

Automation and high-throughput techniques have become increasingly more important throughout bioprocess development for therapeutic proteins. Within Merck's Bioprocess Development organization, we have implemented a fully automated approach to cell line development involving multiple automation systems designed to streamline many of the activities involved in cell line and process development. Here, we will demonstrate how a modular approach to automation allows for increased functionality, flexibility, and overall throughput. With these automation solutions in place, bioprocess development has observed both increased efficiency and productivity across the entire platform.

4:15 End of Conference

Present a Poster & Save!

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by July 18, 2014.

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2nd Annual

Overcoming Formulation Challenges for Biopharmaceutical Development

Optimizing Dosage Form and Process Development for New Biotherapeutics

STREAM 2
Formulation & Downstream Processing

Suggested Short Course*
Accelerated Stability Testing of Biologics
Tuesday, August 19, 6:00-8:30 pm

**Separate registration required; see page 3 for details*

MONDAY, AUGUST 18

8:00 am Pre-Conference Registration and Morning Coffee

9:00-11:30 Short Course*: QbD Strategies for Formulation Development of Protein Therapeutics

**Separate registration required; see page 3 for details*

11:30 Main Conference Registration

CONSIDERATION FOR VACCINES AND NEW BIOLOGICS FORMULATION DEVELOPMENT

1:00 pm Chairperson's Opening Remarks

Mark Yang, Ph.D., Director, Fill Finish Development, Commercial Process Development, Genzyme, a Sanofi Company

1:10 Challenges in Developing Stable Formulations for Vaccines and Biologics

Indresh K. Srivastava, Ph.D., Vice President, Product Realization; Protein Sciences Corp.

The development of a stable formulation is critical for any effective vaccine to prolong its shelf life. One of the major challenges in developing a stable formulation is to ensure that the immunogen is kept in the correct conformation therefore preventing aggregation, degradation etc. and its impact on potency of the vaccine. I will discuss approaches for stabilizing the rHA antigen during the storage. In addition, I will present a case study on the development of a stable formulation for a new biologic.

1:45 Considerations in Formulation Development of DNA-Based Vaccine

Min Huang, Ph.D., Principal Scientist, Pharmaceutical R&D, Pfizer, Inc.

There are unique challenges in formulation development of plasmid DNA based vaccines. Considerations in formulation, stability, viscosity, container closure selection, shipping, process development etc will be discussed. Detailed case studies will be presented to highlight these challenges and share knowledge and technologies that potentially overcome some of these challenges.

2:15 Development of Stable and Efficacious Adjuvanted Protein Vaccines

Yuhong Zeng, Ph.D., Senior Scientist, Alcon Laboratories, Inc.

Besides stability, another challenge for vaccine formulation development is the adsorption of antigens to adjuvant. The effect of antigen-adjuvant interactions on the vaccine efficacy still remains controversial. In this talk, a case study with a smallpox vaccine will be presentedto address these formulation issues. A systematic approach employed in the study to optimize the stability and efficacy of the formulation will be discussed in details.

2:45 Refreshment Break

DEVELOPING QUALITY IN BIOPHARMACEUTICALS

» KEYNOTE PRESENTATIONS:

3:15 Quality by Design Method Development Using a Platform Approach for Multiple Commercial Biological Products

Jianmei Kochling, Ph.D., Director, Quality Science and Analytical Technology, Genzyme, a Sanofi Company

Analytical method development process has evolved along with industry's significant understanding of the "Quality by Design" concept." Quality by design approach analytical methods development relies upfront understanding of targeted method attributes and acceptance criteria, process and product knowledge, and the incorporation of the modern technology. In this presentation, the method development process as well as case studies will be presented for the QbD methods development using a platform approach.

3:45 Panel Discussion: Consideration and Expectations for Assessing Quality and Stability of Biopharmaceuticals

- Current regulatory requirements vs. requirement 10 years ago
- Implications of improved method quality with new technologies vs. continuous use of the old technologies
- Requirements for early stage vs. late stage development

Moderator:
Mark Yang, Ph.D., Director, Fill Finish Development, Commercial Process Development, Genzyme, a Sanofi Company
Panelists:
Paul Bigwarfe, Jr., Ph.D., Director, Analytical Sciences, Industrial Operations and Product Supply, Regeneron Pharmaceuticals, Inc
Ernesto Freire, Ph.D., Professor, Biology and Biophysics, Johns Hopkins University
Jianmei Kochling, Ph.D., Director, Quality Science and Analytical Technology, Genzyme, a Sanofi Company
Aleš Štrancar, Ph.D., CEO, BIA Separations GmbH

4:15 Breakout Discussions

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. At the end of the session, each moderator will summarize the topics being discussed, the findings and conclusions (if any), and share with the audience.

5:15 Discussion Report-Outs

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2nd Annual

Overcoming Formulation Challenges for Biopharmaceutical Development

STREAM 2
Formulation & Downstream Processing

Optimizing Dosage Form and Process Development for New Biotherapeutics

5:30 Grand Opening Reception in the Exhibit Hall with Poster Viewing

7:00 End of Day

TUESDAY, AUGUST 19

7:30 am Registration and Morning Coffee

CHALLENGES IN PROCESS DEVELOPMENT & FILL FINISH OPERATIONS

7:55 Chairperson's Remarks
Paul DiGregorio, Ph.D., Director, Strategic Accounts, Freeslate, Inc.

8:00 Strategy for Mitigating Particulate Risks during Product Manufacturing and Clinical Administration of a Biologic for Use in Phase I Clinical Studies
Zhiqing Zhu, Ph.D., Research Investigator, Drug Product Science and Technology Department, Bristol-Myers Squibb Co.
Protein particulate formation often presents a challenge to drug product development process, especially during manufacturing operations and clinical compounding and administration. Here, we present a case study where phase-appropriate approaches (e.g. scale-down model, syringe/needle combination selection) were utilized to facilitate the successful development of a biologic for use in Phase I studies. Although the molecule had a history of particulate formation, the approaches adopted successfully and can be readily applied or adapted to similar situations.

8:30 Protein Oxidation during Formulation and Fill Finish Operations
Mark Yang, Ph.D., Director, Fill Finish Development, Commercial Process Development, Genzyme, a Sanofi Company
Hydrogen peroxide (HP) is present ubiquitously in water and excipients, and is generated by formulation and fill finish processes. Even at sub-ppm concentration, HP can cause significant protein oxidation and impact drug product quality. HP spiking study is often used to evaluate the effect of residual HP on a given protein formulation. Data from a new spiking study will be presented.

9:00 Challenges in the Filtration of High-Concentration Formulations during Fill Finish Operations
Curtiss P. Schneider, Ph.D., Senior Engineer I, Protein Pharmaceutical Development, Biogen Idec
Late stage changes in equipment and process design for fill finish operations can result in filtration challenges that are often not well understood or previously observed. In the case study presented here, an overview is given for a filter fouling event never before seen during the manufacture of a high-concentration mAb product. A combination of tank mixer configuration, contact interfaces, and hold times will be discussed as implicated root causes for the observation.

9:30 Selected Poster Presentation: Application of Formulatrix Liquid Handler in Protein Formulation Development
Adnan Zunic, Senior Associate Scientist, Protein Pharmaceutical Development, Biogen Idec
In this talk, the use of the Formulatrix's Formulator liquid handling system as an aid in protein formulation development (for solubility and excipient screens) will be described.

9:45 Coffee Break in the Exhibit Hall with Poster Viewing

HIGH-THROUGHPUT MEASURES TO OVERCOME FORMULATION CHALLENGES

10:30 Lipase Hydrolysis of Polysorbate 80 in High Concentration mAb Formulations
Steven LaBrenz, Ph.D., Scientific Director, Drug Product Development, Janssen R&D

11:00 High-Throughput Study Designs to Evaluate and Overcome Protein Instabilities
Wayne F. Reed, Ph.D., Murchison Mallory Chair Professor of Physics, Department of Physics, Tulane University
SMSLS measured real-time aggregation kinetics of several proteins under thermal and stir stressors up to concentrations >0.100g/cm3. Arrhenius behavior is found for thermal data, but there is no relationship between aggregation rates, which vary by >106, and Tm and unfolding activation energy. Rates under stir are surprisingly similar. Stirring effects of enhanced air/liquid interface exposure vs. mechanical shear were separated. Thermal and stirring aggregation mechanisms are different. The appearance of particulates during aggregation was monitored.

11:30 Automated, High-Throughput Approaches to Protein Formulation
Sponsored by freeslate
Paul DiGregorio, Ph.D., Director, Strategic Accounts, Freeslate, Inc.
Case studies that examine the utilization of automated, high-throughput systems with integrated analytics to assess protein formulations.

11:45 Sponsored Presentations
(Opportunities Available)

12:30 pm Luncheon Presentation
(Sponsorship Opportunity Available)
or Lunch on Your Own

1:15 Session Break

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Overcoming Formulation Challenges for Biopharmaceutical Development

STREAM 2
Formulation & Downstream Processing

Optimizing Dosage Form and Process Development for New Biotherapeutics

RAPID SCREENING IN EARLY BIOTHERAPEUTIC DEVELOPMENT

1:55 Chairperson's Remarks

Wayne F. Reed, Ph.D., Murchison Mallory Chair Professor of Physics, Department of Physics, Tulane University

2:00 Alternative Methods for Quantifying Temperature- and Formulation-Dependent Aggregation Rates

Christopher J. Roberts, Associate Professor, Department of Chemical & Biomolecular Engineering, University of Delaware

Reliably predicting protein aggregation rates from accelerated storage conditions remains an outstanding challenge for formulation scientists. Issues that need to be overcome include: sufficiently accurate means to quantify how rates change with storage condition and non-linear effects that make extrapolations difficult to perform accurately. This talk presents illustrative methods to improve predictions of aggregation rates, with monoclonal antibodies as case studies, and also highlights remaining challenges for future efforts.

2:30 The Measurement of KD at Low Concentration and Its Application as a High-Throughput Screening Technique for Protein-Protein Interaction Measurements

Anthony L. Young, Ph.D., Principal Scientist, Pharmaceutical Research and Development, Pfizer, Inc.

The light scattering measurement is routinely run in a high-throughput format to quickly determine the necessary diffusion coefficient versus concentration curves. The use of a robotic liquid handler can reduce the preparation time of the dilution sequence. This talk will cover the use of the liquid handler in combination with the dynamic light scattering instrument to generate KD values that are used to screen proteins and protein formulations for development. The data from several different protein isoforms will be discussed to illustrate the screening process and show typical data.

3:00 Simultaneous Stability and Aggregation Assessment by Isothermal Chemical Denaturation

Ernesto Freire, Ph.D., Professor, Biology and Biophysics, Johns Hopkins University

Stability and aggregation are two of the most important hurdles in the formulation of biologicals. Isothermal chemical denaturation (ICD) provides the most accurate way of measuring protein stability at room, physiological or storage temperatures under different solvent or formulation conditions, yielding reliable thermodynamic stability parameters. Furthermore, ICD experiments performed at different protein concentrations provide a quantitative assessment of protein aggregation in the native and denatured states. ICD is ideally suited to optimize the formulation of proteins hard to formulate, highly concentrated formulations, bispecific antibodies and antibody drug conjugates. In this presentation, the fundamentals of ICD and its application to the evaluation of protein stability and optimization of formulation conditions will be discussed.

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

4:15 Application of DSF as a High-Throughput Tool in Protein Characterization and Formulation Development

Shuai "Sunny" Shi, Ph.D., Senior Scientist, Sterile Product Development, Merck

In this study, we benchmarked DSF against the conventional thermal technique, differential scanning calorimetry (DSC), and more importantly made an attempt to predict protein thermal aggregation kinetics by DSF. We have defined three levels of correlations between DSF/DSC transition temperature and real-time thermal aggregation kinetics which will be shown in 3 individual case studies. We will also demonstrate the unique application of DSF in studying concentration-dependent thermal behaviors especially in the high-concentration range.

4:45 Increasing the Throughput of Protein Formulation Screening Using 96-Well Plate Format

Qingyan Hu, Scientist, Ph.D., Scientist, Formulation Development, Regeneron, Inc.

To increase throughput during formulation screening, the use of a 96-well plate format was explored for candidate selection and formulation development. Multiple mAb candidates were screened against different buffer/pH and excipients using the 96-well plate format. In addition, the stability study results obtained using the 96-well plate format was compared to the results from using glass vials. With the incorporations of an automated liquid handling system and analytical instruments compatible with 96-well plates, this approach would greatly increase the throughput of formulation screening and development.

5:15 End of Conference

5:15-6:00 Dinner Short Course Registration

6:00-8:30 Dinner Short Course*: Accelerated Stability Testing of Biologics

*Separate registration required; see page 3 for details

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3rd Annual

Overcoming Challenges in High Viscosity, Aggregation and Stability

STREAM 2
Formulation & Downstream Processing

Suggested Short Course*:
Bioprocess Development: Considerations for the Quality and Safety of Materials in Contact with Biologics
Thursday, August 21, 6:30 - 9:00 pm

Separate registration required; see page 3 for details

WEDNESDAY, AUGUST 20

7:00 am Registration and Morning Coffee

PROTEIN ASSOCIATION AND AGGREGATION

8:05 Chairperson's Remarks
Dean Ripple, Ph.D., Leader, Bioprocess Measurements Group, National Institute of Standards and Technology

» KEYNOTE PRESENTATIONS

8:15 Mechanisms of Protein Association and Aggregation
Thomas Laue, Ph.D., Professor, Biochemistry and Molecular Biology; Director, Biomolecular Interaction Technologies Center (BITC), University of New Hampshire
The same forces underlie protein stability, protein-protein interactions and protein aggregation. In addition to viewing the thermodynamics of these processes, it is worthwhile to consider their kinetic aspects. A kinetic view of these processes is particularly revealing with respect to hydrophobic interactions. Considering hydrophobic interactions as a two-step process that first involves de-solvation, then dispersion-energy stabilization leads to the conclusion that flanking hydrophobic regions with anionic groups should reduce hydrophobically-driven aggregation.

9:00 Liquid-Liquid Phase Separation as a Quantitative Colloidal Stability Assay for Monoclonal Antibodies
Ramil F. Latypov, Ph.D., Principal Scientist, Process & Product Development, Amgen, Inc.
Colloidal stability is an important consideration in formulation development of therapeutic antibodies. In a protein solution, different pathways including crystallization, aggregation and liquid-liquid phase separation (LLPS) can lead to the formation of precipitates and particles. Polyethylene glycol (PEG) induces LLPS in antibody solutions and can be used to compare colloidal stability of antibodies in different conditions. Our analysis defines the binding energy in the PEG-induced condensed phase to quantitatively measure attractive interactions between antibody molecules.

9:30 Structural and Surface Characteristics of a Protein that Impact its Opalescence in Solution
Ravi Chari, Ph.D., Senior Scientist, Pharmaceutics, AbbVie Bioresearch Center
In this study we investigated the underlying properties of a protein that led to its opalescence in solution. Initial formulation studies led to the hypothesis that hydrophobic interactions governed this behavior. Computer modeling was then performed to identify hydrophobic residues and surfaces of the protein that could be targeted for mutational studies to test the hypothesis. The results suggest that the degree and nature of hydrophobicity impacted opalescence.

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

10:45 Monoclonal Antibody Self-Association, Rheology, and Phase Behavior at High Concentrations
Wenhua Wang, Ph.D., Postdoctoral Fellow, Late Stage Pharmaceutical Development, Genentech, Inc.
Therapeutic protein intermolecular interactions at high concentrations often lead to manufacturing problems including high viscosity, turbidity, and aggregation. Here, we presented our work on the correlation of monoclonal antibody (mAb) self-associating dimer and oligomer structural information to their rheology and phase behaviors. A better understanding of mAb self-association behaviors from this research is insightful not only for overcoming challenges in high-concentration protein formulations, but also for comprehending the mechanisms of protein gelation or crystal formation.

11:15 CMC Challenges in Development of High Concentration Protein Formulation
Jamie Tsung, Ph.D., Principle Scientist, Momenta Pharmaceuticals, Inc.
Highly concentrated therapeutic proteins are prone to be viscous and aggregate posing developmental and CMC challenges in purification, formulation, analytical development, manufacturing, product stability, syringeability and injectability. This talk provides a review of current strategies and technologies used in product development to overcome these CMC challenges and minimize the impact on product quality.

11:45 Selected Poster Presentation: Opalescence in a Monoclonal Antibody Solution and Its Correlation with Intermolecular Interactions in Dilute and Concentrated Solutions
Ashlesha S. Raut, Ph.D. Candidate, Department of Pharmaceutical Sciences, University of Connecticut
Monoclonal antibody molecule studied, shows a unique property of high opalescence due to liquid-liquid phase separation. Results indicate that high opalescence and phase separation are due to the attractive interactions in solution as measured using light scattering and rheology, however, presence of attractive interactions do not always imply phase separation. Temperature dependence of opalescence, suggests that Tcloud can be utilized as a potential tool to assess attractive interactions in solution.

12:15 pm Luncheon Presentation
(Sponsorship Opportunity Available)

1:30 Session Break

OVERCOMING AGGREGATION & VISCOSITY CHALLENGES

1:55 Chairperson's Remarks
Ramil F. Latypov, Ph.D., Principal Scientist, Process & Product Development, Amgen, Inc.

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High-Concentration Protein Formulations

Overcoming Challenges in High Viscosity, Aggregation and Stability

STREAM 2
Formulation & Downstream Processing

2:00 Multimer Protein Cluster Structure at High-Concentration: Dynamic Modeling of Stability and Viscosity

John Tsavalas, Ph.D., Assistant Professor of Materials Science, University of New Hampshire

In this work, a dynamic model is presented that can evaluate and predict this behavior of proteins in concentrated solutions as a function of their charge, charge distribution, and resultant interaction potential. In particular, the viscosity response to the stability of the proteins in solution is discussed with emphasis on the effective hydrodynamic radius due to the high aspect ratio of a mAb exacerbated by weak clustering of multiple mAbs during concentration.

2:30 Understanding and Addressing Viscosity in the Development of High-Concentration Protein Formulations

Robert H. Walters, Senior Scientist, Biotherapeutics Pharmaceutical R&D, Pfizer, Inc.

High-concentration formulations of therapeutic proteins are beneficial as they reduce storage costs of biotherapeutics and can enable more patient friendly administration options, such as subcutaneous dosing. However, development of high-concentration formulations remains challenging. High viscosities associated with high-concentration protein formulations can negatively impact manufacturability and injectability of the product. This talk will focus on understanding the sources of elevated viscosity in high-concentration protein formulations and suggest strategies for viscosity reduction.

3:00 Instrument Biases for Counting and Sizing of Particles in High-Concentration Formulations

Dean Ripple, Ph.D., Leader, Bioprocess Measurements Group, National Institute of Standards and Technology

Characterization and sizing of protein particles is necessary for assuring the quality of drug products. High-concentration formulations lead to reduced optical contrast of particles, leading to errors for the most common optical methods of particle detection. This talk discusses biases between methods in common use, as identified by the NIST round robin comparison on subvisible particles, and then considers the impact of either high protein or high excipient concentrations on these biases.

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

EMERGING BIOPHYSICAL TECHNIQUES FOR HIGH-CONCENTRATION FORMULATIONS

4:15 Orthogonal Toolbox for Screening and Identification of High-Concentration mAb Formulations

Yunsong "Frank" Li, Ph.D., Associate Principal Scientist, Bioprocess Development, Merck Research Laboratories

In this study, we focused on the evaluation of several techniques for understanding of high-concentration mAb solution properties. We observed good correlations between turbidity, relative solubility and the second viral coefficient (B22) value which are indicative of protein colloidal stability. We have demonstrated the ability of DSF to test high concentration protein formulations and comparison between classical formulation stability studies and new toolbox will also be presented for 150 mg/mL mAb formulations.

4:45 Extended Q&A with Speakers

5:15 Networking Reception in the Exhibit Hall with Poster Viewing

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6:30 End of Day

THURSDAY, AUGUST 21

8:00 am Registration and Morning Coffee

DEVELOPMENT & MANUFACTURING OF HIGH CONCENTRATION FORMULATIONS

8:25 Chairperson's Remarks

Jan Jezek, Ph.D., CSO, Development, Arecor Ltd.

8:30 Challenges in Developing High-Concentration Liquid Formulations for Novel Biologics Formats: Fusion Protein, Bi-Specifics

Kapil Gupta, Ph.D., Senior Fellow, Integrated Biologics Profiling, Novartis Institute of Biomedical Research

In recent years, the biologics pipeline in many organizations is maturing from simple monoclonal antibodies to more complex molecular formats such as Fc-fusion, bi-specifics and multifunctional molecules. These new formats demonstrate superior biological characteristics but bring significant challenges in high-concentration liquid formulation development due to unfavorable physical-chemical properties. This talk will provide an overview of challenges encountered in formulation developability assessment of novel biologics formats.

9:00 Manufacturing High-Concentration Monoclonal Antibody (mAb) Formulations via Spray Drying Technology

Yuh-Fun Maa, Ph.D., Principal Engineer, Pharmaceutical Processing & Technology Development, Genentech, Inc.

This study evaluated a pilot-scale spray dryer against a laboratory-scale dryer to spray dry multiple mAbs in consideration of scale-up, process optimization, impact on mAb stability, and feasibility of a high-concentration preparation. The outcome of the study demonstrated mAb chemical/potency stability, performance comparability of the scaled-up process, and the ability of concentrating mAb to >300 mg/mL This study offers a commercially viable spray-drying process for high-concentration mAb manufacturing option.

9:30 Challenges in Developing High-Concentration Stable Formulation for Biologics

Indresh K. Srivastava, Ph.D., Vice President, Product Realization, Protein Sciences Corp.

The development of a stable formulation is critical for any effective vaccine or biologics to prolong its shelf life, maintain its functionality, and efficacy. Most of the biologics are needed at a very high concentration for clinical and logistical reasons. One of the major challenges in developing a stable formulation for biologics at high conc. is how to prevent the protein from aggregation/precipitation therefore loosing its potency and clinical efficacy. I will present a case study on the development of a high-concentration formulation.

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High-Concentration Protein Formulations

Overcoming Challenges in High Viscosity, Aggregation and Stability

STREAM 2
Formulation & Downstream Processing

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

ADMINISTRATION CHALLENGES OF HIGH-CONCENTRATION FORMULATION

10:45 Overcoming the Need for High Protein Concentrations for Subcutaneous Drug Delivery Using a Novel Excipient

David Gold, Ph.D., Associate Director, Business Development, Halozyme Therapeutics

Traditional subcutaneous drug delivery for biologics can require highly concentrated formulations in order to minimize the volume administered. Addition of a novel recombinant hyaluronidase excipient (rHuPH20) to the formulation can allow for larger volumes to be delivered. This excipient opens up channels within the subcutaneous space by depolymerizing its target substrate, hyaluronan. Further, the molecule has been shown to be compatible with a wide range of biologics, including antibodies, peptides and other therapeutic proteins.

11:15 Alternative Methods of Formulating High-Concentration Proteins to Overcome Administration Challenges

Jan Jezek, Ph.D., CSO, Development, Arecor Ltd.

With increasing competition in the biopharmaceutical market there is a strong trend toward improving convenience of administration. A switch from intravenous infusion to a convenient subcutaneous injection often requires an increase in protein concentration, leading to stability and injectability issues. The talk will describe innovative approaches, to processing and formulating concentrated protein compositions to enable development of commercially viable products. The novel approaches also have a benefit of additional IP protection of the resulting products.

11:45 Challenges in Reconstitution of High-Concentration Protein Formulations

Pooja Sane, Doctoral Candidate, Department of Pharmaceutical Sciences, School of Pharmacy, University of Connecticut

Co-Developed by: Robin Bogner, Ph.D., Associate Professor, Department of Pharmaceutical Sciences, School of Pharmacy, University of Connecticut

Lyophilized highly concentrated protein formulations are notorious for their long reconstitution times posing problem for administration to patients. Several strategies have been reported to reduce the reconstitution times. A review of those strategies and our analysis of the wetting behavior, hydration and disintegration rates to identify potential causes of long reconstitution times will be presented.

12:15 pm Sponsored Presentation
(Opportunity Available)

12:30 Luncheon Presentation
(Sponsorship Opportunity Available)

1:15 End of Conference

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Advances in Purification Technologies

Advanced Technologies & Novel Concepts in Protein Purification & Recovery

STREAM 2
Formulation & Downstream Processing

Suggested Short Course*

ABC: Anything But Chromatography – Precipitation, Crystallization and Flocculation

Thursday, August 21, 6:30 – 9:00 pm

Separate registration required; see page 3 for details

THURSDAY, AUGUST 21

1:55 pm Chairperson's Remarks

Greg Zarbis-Papastoitsis, Ph.D., Vice President, Process and Manufacturing Sciences, Eleven Biotherapeutics

» 2:00 KEYNOTE PRESENTATION

Cold Ethanol Precipitation and Flocculation for Continuous Downstream Processing of Recombinant Antibodies

Alois Jungbaer, Ph.D., Professor, Department of Biotechnology, University of Natural Resources and Life Science Vienna, (BOKU) and Austrian Centre of Industrial Biotechnology

We have developed a completely new, non-chromatographic alternative based on a series of selective precipitation and flocculation steps. Our process does not need elution chromatography anymore. The method is a generic platform technology and has been tested in the purification of several human antibodies with different pI and hydrophobicity. The full potential of this new continuous downstream technology can be harnessed by coupling to a continuous upstream process/perfusion reactor. Examples for fully continuous operating reactors will be shown.

NEW APPROACHES AND TECHNOLOGIES IN PURIFICATION CHROMATOGRAPHY

2:45 Dramatic Improvements in Process Economy with Non-Column Purification

*Richard Nian, Ph.D., Research Scientist, Downstream Processing Group, Bioprocess Technology Institute, A*Star, Singapore*

In this study, we show data from new clarification methods that enable a number of non-protein A capture alternatives, including non-column formats. We also show data from a breakthrough convection-based system that supports 10-fold lower host protein, aggregate and DNA content, plus 10-20% higher IgG recovery compared to 3-step protein A platforms. And it achieves these results with two thirds less water than current protein A platforms.

3:15 A Designed Calcium-Responsive Peptide Domain for Non-Chromatographic Protein Purification

Scott Banta, Ph.D., Associate Professor, Chemical Engineering, Columbia University

We have discovered a peptide sequence based on the beta-roll forming RTX domain that reversibly precipitates in the presence of calcium. We have developed this phase-change as a simple method for the non-chromatographic purification of recombinant proteins. We have demonstrated this technique with several model proteins, and the technique should be broadly applicable.

3:45 Implementing 45 cm ID Pre-Packed Columns for GMP Manufacturing

Sponsored by RepliGen BIOPROCESSING

Fletcher Malcom, MBA, Associate Director, Product Management, Repligen Corporation

Implementation of pre-packed disposable columns is increasing as the technology advances to deliver more options for GMP manufacturing operations which rely on disposable components. This presentation explores the new technological developments as well as the benefits of larger 45 cm ID pre-packed chromatography columns.

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

4:45 Breakout Discussions

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. At the end of the session, each moderator will summarize the topics being discussed, the findings and conclusions (if any), and share with the audience.

5:45 End of Day

5:45 – 6:30 Dinner Short Course Registration

6:30 – 9:00 Dinner Short Course*: ABC: Anything But Chromatography

FRIDAY, AUGUST 22

8:00 am Registration and Morning Coffee

NEW APPROACHES AND TECHNOLOGIES IN PURIFICATION CHROMATOGRAPHY (cont.)

8:25 Chairperson's Remarks

Alois Jungbaer, Ph.D., Professor, Department of Biotechnology, University of Natural Resources and Life Science Vienna, (BOKU) and Austrian Centre of Industrial Biotechnology

8:30 Design and Optimization of Countercurrent Tangential Chromatography for Monoclonal Antibody Purification

Andrew Zydney, Ph.D., Professor and Department Head, Chemical Engineering, The Pennsylvania State University

Countercurrent Tangential Chromatography (CTC) is a new column-free capture technology that enables fully disposable operation. Binding, washing, elution, stripping, and equilibration steps are conducted on a moving slurry pumped continuously through a cascade of static mixers and hollow fiber membrane modules. This talk will describe the analysis used to develop and optimize a CTC system for monoclonal antibody purification that provides comparable antibody yield and host cell protein removal with nearly 10-fold greater productivity than conventional packed columns.

9:00 Bench-Scale Development of a Multi-Column Continuous Protein A Affinity Process For mAb Biomanufacture

Anthony Grabski, Ph.D., Director, R&D, Semba Biosciences, Inc.

We tested multi-column continuous chromatography (MCC) protocols for Protein A affinity purification of monoclonal antibodies (mAbs). We will present results comparing various protocols and adsorbents for their productivity and efficacy in an 8-column MCC process. The relationship between mAb titer and productivity with MCC vs. the traditional batch process will be experimentally demonstrated.

9:30 The Use of Multi-Modal Chromatography for the Removal of Aggregates and Protein Impurities

Shuang Chen, Ph.D., Senior Scientist, Pfizer, Inc.

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Advances in Purification Technologies

Advanced Technologies & Novel Concepts in Protein Purification & Recovery

STREAM 2
Formulation & Downstream Processing

10:00 Mid-Morning Snack in the Exhibit Hall with Poster Viewing

10:45 A Non Protein-A Capture Step for mAbs Based on Selective Precipitation Combined with CEX

Danielle van Wijk, Ph.D., Project Leader, Downstream Processing, Synthon Biopharmaceuticals

A low cost and non toxic precipitation agent was used combined with a novel cationic (CEX) resin as the initial purification step. Several CEX resins were evaluated for binding capacity, selectivity and cleanability. The selected CEX resin has a significant increased capacity over protein A and data indicate a combined use of selective precipitation and CEX are promising for future "high" titer antibody purification processes.

11:15 Fast Track Process Development and Validation: Chromatographic High-Throughput Characterization - Is This the Solution for Process Development?

Matteo Costioli, Ph.D., DSP Process Development Manager, BioProcess Science, Merck Serono

To rapidly develop a safe, well controlled, efficient and cost effective process, the use of HTS combined with design of experiment, is key. A case study for a MAb of a fast track process development approach for a CEX step is discussed. A proposed characterization using micro- column in combination with a robotic liquid handling system and the ensuing scale-up to lab-scale is described. Implementation of a HTS in the new 3 stage process validation framework is also discussed.

11:45 Hydrophobic Interaction Chromatography Optimization Using Definitive Screening Design Versus Traditional Experimental Designs

Yi Li, Ph.D., Sr. Scientist, Biologic Process Development, Bristol-Myers Squibb

The optimization of hydrophobic interaction chromatography (HIC) can consume a considerable amount of material and time using traditional experimental designs. Definitive screening design (DSD) uses fewer experiments to identify significant factors to provide resolution between main effects, two-way interactions and quadratic effects. We optimized ten HIC parameters for protein recovery and aggregate clearance using high-throughput chromatography. Results show the robustness of DSD and important findings were confirmed.

12:15 High Throughput Optimization Approach for Single Step Polishing of Monoclonal Antibodies Post Protein A Capture

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Ian Sellick, Director, Marketing, Pall Life Sciences

12:30 Sponsored Presentation *(Opportunity Available)*

12:45 Luncheon Presentation *(Sponsorship Opportunity Available)*

TECHNIQUES AND STRATEGIES TO OVERCOME PURIFICATION AND CLARIFICATION CHALLENGES

1:25 Chairperson's Remarks

Sophia T. Mundle, Ph.D., Senior Manager, Protein Chemistry, Sanofi Pasteur

1:30 Viral Clearance Challenges in mAb Development

Joe Zhou, Ph.D., CEO, Genor Biopharma, Walvax Bio Group and Visiting Professor, Peking University

2:00 Clarification and Purification Techniques for High Density Mammalian Cell Cultures and Bacterial Fermentation

Kathryn Golden, MEng., Scientist II/Development Project Manager, Manufacturing and Process Sciences, Eleven Biotherapeutics

State-of-the-art upstream processes continue to push industry limits with increasingly concentrated cell densities and productivities in both mammalian cell culture and bacterial fermentation. Associated improvements in clarification and purification techniques are being designed to handle these challenging process streams. Two case studies of the development of high density upstream, clarification, and purification processes will be discussed.

2:30 Purification of the Sanofi Pasteur HSV2 Vaccine Candidate, HSV529

Sophia T. Mundle, Ph.D., Senior Manager, Protein Chemistry, Sanofi Pasteur

The Sanofi Pasteur replication defective HSV2 vaccine candidate, HSV529, can be purified by a method which includes a combination of harvesting without cell disruption, endonuclease treatment, depth filtration, anion-exchange chromatography and ultrafiltration/diafiltration (UF/DF). The resultant virus retains infectivity and is ~ 200-fold more pure with respect to host cell DNA and proteins than is HSV529 purified by ultracentrifugation. Side-by-side comparison of chromatography-purified ACAM529 with sucrose cushion-purified HSV529 shows that both preparations are equally immunogenic and protective when tested *in vivo*.

3:00 Refreshment Break

3:15 High-Throughput Ion Exchange Purification of Positively Charged Recombinant Protein in the Presence of Negatively Charged Dextran Sulfate

Lam Markely, Scientist II, Cell Culture Development – High-Throughput Analytical Group, Biogen Idec

We developed an SSP (small scale protein purification) using ion exchange resins to purify positively charged recombinant growth factor P1 in the presence of negatively charged dextran sulfate. The major challenge in this work is that strong ionic interaction between P1 and dextran sulfate disrupts interaction between P1 and chromatography resins. To solve this problem, we develop a two-step SSP using Q Sepharose Fast Flow (QFF) and SP Sepharose XL (SPXL) resins to purify P1.

3:45 Protein Glycosylation Selectivity in Chromatographic Separation

Alan Shupe, Ph.D., Scientist I, Biologics Manufacturing and Process Development, Bristol-Myers Squibb

Variation in glycan components such as sialic acid exhibit different local charge density and hydrophobicity, and affect the purification performance. In this study we examine the separation behaviors of monomeric and high-molecular weight glycoforms in both ion-exchange (IEX) and hydrophobic interaction (HIC) chromatography. The interplay between IEX and HIC profiles becomes self-evident when analyzing all types of glycoforms together. This study illustrates some general aspects about how glycosylation heterogeneity can impact product quality and process yield.

4:15 Next-Generation Purification Processing: A Comparison of Novel Approaches for Integrated and High-Throughput Processing

Finn Hung, Ph.D., Senior Scientist, Merck & Co.

4:45 End of Conference

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2nd Annual

Rapid Methods to Assess Quality & Stability of Biologics

Improving Prediction and Screening

STREAM 3
Analytical Development & Quality

Suggested Short Course*

Accelerated Stability Testing of Biologics

Tuesday, August 19, 6:00-8:30 pm

*Separate registration required; see page 3 for details

MONDAY, AUGUST 18

8:00 am Pre-Conference Registration and Morning Coffee

9:00 – 11:30 Short Course*: QbD Strategies for Formulation Development of Protein Therapeutics

*Separate registration required; see page 3 for details

11:30 Main Conference Registration

RAPID METHODS FOR COMMERCIAL QUALITY CONTROL LABS

1:00 pm Chairperson's Opening Remarks

Jianmei Kochling, Ph.D., Director, Quality Science and Analytical Technology, Genzyme, a Sanofi Company

1:10 Rapid Analytical Techniques for the Commercial Quality Control Laboratories in Preparation for Regulatory Filings

Paul Bigwarfe, Jr., Ph.D., Director, Analytical Sciences, Industrial Operations and Product Supply, Regeneron Pharmaceuticals, Inc.

Many new technologies are becoming amenable to the commercial QC laboratory, and their implementation requires special consideration. Using the example of new molecular sizing methods (UPLC and capillary CE based), analytical transfer, validation, method bridging, and specification setting issues will be discussed. In addition, examples of how to introduce assay controls and write procedures for use in a GMP commercial lab will be provided.

1:45 Introduction of PAT to Improve the Efficiency and Robustness of Biopharmaceutical Manufacturing

Sponsored by BIA separations

Aleš Štrancar, Ph.D., CEO, BIA Separations GmbH

During the development of up- or down-stream process of biomolecules, it is essential to have fast, accurate and reliable analytical methods. Examples of PAT in biopharmaceutical manufacturing by using specially designed monolithic HPLC columns, supplied by Agilent or by BIA Separations, to provide rapid, actionable information about the quantity and purity of target molecules in different feed stream samples, will be presented.

2:15 High-Throughput Method Development for Product Stability and Impurity Evaluation

Zhenyu Gu, Ph.D., Development Scientist II, Analytical Sciences, Alexion Pharmaceuticals, Inc.

High-throughput analytical methods were developed to evaluate product related impurity, stability and process related impurity. In addition to high-throughput, the new methods demonstrated less assay induced artifacts than the traditional methods. Protein degradation products were characterized by the new method in a much reliable way. Levels of several process-related impurities were determined simultaneously by the new methods because of the good resolution. Previously, each impurity had to be analyzed individually by the corresponding traditional method.

2:45 Refreshment Break

DEVELOPING QUALITY IN BIOPHARMACEUTICALS

» KEYNOTE PRESENTATIONS

3:15 Quality by Design Method Development Using a Platform Approach for Multiple Commercial Biological Products

Jianmei Kochling, Ph.D., Director, Quality Science and Analytical Technology, Genzyme, a Sanofi Company

Analytical method development process has evolved along with industry's significant understanding of the "Quality by Design" concept". Quality by design approach analytical methods development relies upfront understanding of targeted method attributes and acceptance criteria, process and product knowledge, and the incorporation of the modern technology. In this presentation, the method development process as well as case studies will be presented for the QbD methods development using a platform approach.

3:45 Panel Discussion: Consideration and Expectations for Assessing Quality and Stability of Biopharmaceuticals

- Current regulatory requirements vs. requirement 10 years ago
- Implications of improved method quality with new technologies vs. continuous use of the old technologies
- Requirements for early stage vs. late stage development

Moderator:

Mark Yang, Ph.D., Director, Fill Finish Development, Commercial Process Development, Genzyme, a Sanofi Company

Panelists:

Paul Bigwarfe, Jr., Ph.D., Director, Analytical Sciences, Industrial Operations and Product Supply, Regeneron Pharmaceuticals, Inc

Ernesto Freire, Ph.D., Professor, Biology and Biophysics, Johns Hopkins University

Jianmei Kochling, Ph.D., Director, Quality Science and Analytical Technology, Genzyme, a Sanofi Company

Aleš Štrancar, Ph.D., CEO, BIA Separations GmbH

4:15 Breakout Discussions

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. At the end of the session, each moderator will summarize the topics being discussed, the findings and conclusions (if any), and share with the audience.

5:15 Discussion Report-Outs

5:30 Grand Opening Reception in the Exhibit Hall with Poster Viewing

7:00 End of Day

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Rapid Methods to Assess Quality & Stability of Biologics

Improving Prediction and Screening

STREAM 3
Analytical Development & Quality

TUESDAY, AUGUST 19

7:30 am Registration and Morning Coffee

RAPID ASSESSMENT OF PARTICLES, AGGREGATION & STABILITY

7:55 Chairperson's Remarks

Nanda Subbarao, Ph.D., Senior Consultant, Analytical CMC, Biologics Consulting Group

8:00 Methods for Rapid Assessment of Aggregation and Particle Formation

Dean Ripple, Ph.D., Leader, Bioprocess Measurements Group, National Institute of Standards and Technology

Rapid assessment of the formation of particles in drug candidates requires the use of analytical methods that are suited to high throughput. Four main types of methods are considered: static and dynamic light scattering, static and dynamic microscopic imaging, temperature scanning methods with either calorimetric or fluorescent detection, and prospects for new, novel methods. For each method, I discuss the applicable size range, the sensitivity, and various advantages and disadvantages.

8:30 Emerging Methods for Measuring Sub Visible Particles

Nanda Subbarao, Ph.D., Senior Consultant, Analytical CMC, Biologics Consulting Group

The tools available for analysis of sub-visible particles in well-characterized protein products have increased over the past years in response to gradually increasing regulatory expectations to test for them. These emerging methods are based on different technologies. Therefore use of these methods together will provide a more complete description of the sub-visible particles, however the results cannot always be compared directly because they evaluate different features of the particles. The advantages and disadvantages of the different methods will be discussed.

9:00 Evaluation of the Stability of Low Concentration Maytansinoid ADCs in Infusion Bags and their Compatibilities with Administration Sets

Joyce Lin, Senior Research Associate, Analytical and Pharmaceutical Sciences, ImmunoGen, Inc.

Maytansinoid ADCs (AMCs) are used for the treatment of cancer. The AMC drug products are placed into infusion bags that contain appropriate diluent and administered intravenously. The stability of the AMCs and their compatibilities with the administration sets need to be evaluated before the start of the clinical trials. The human starting dose levels are relatively low and pose challenges during the assessment of compatibility of the diluted AMCs with infusion sets.

9:30 Q&A with Speakers

9:45 Coffee Break in the Exhibit Hall with Poster Viewing

10:30 Recent Advances in Monitoring Protein Aggregation Kinetics and Mechanisms with Simultaneous Multiple Sample Light Scattering (SMSLS)

Wayne F. Reed, Ph.D., Murchison Mallory Chair Professor of Physics, Department of Physics, Tulane University

SMSLS measured real-time aggregation kinetics of several proteins under thermal and stir stressors up to concentrations >0.100g/cm3. Arrhenius behavior is found for thermal data, but there is no relationship between aggregation rates, which vary by >106, and Tm and unfolding activation energy. Rates under stir are surprisingly similar. Stirring effects of enhanced air/liquid interface exposure vs. mechanical shear were separated. Thermal and stirring aggregation mechanisms are different. The appearance of particulates during aggregation was monitored.

11:00 Poly-Specificity as an Early Metric for Antibody Developability

Eric Krauland, Ph.D., Senior Director, Antibody Discovery and Optimization, Adimab LLC

The developability of antibody therapeutics is a historically overlooked aspect in the early discovery process. To this end, we demonstrate that a simple flow cytometry-based poly-specificity assay predicts poor CMC properties by correlation to validated characterization techniques. But unlike these assays, the flow cytometry poly-specificity assay is also compatible with active selection from large and diverse antibody mixtures. Selecting for CMC properties and target biology in the earliest discovery stages aims to improve the efficiency of the overall development process.

11:30 Selected Poster Presentation: Endotoxin Contamination in BioPharmaceuticals: Overcoming False Negative Results Induced by Endotoxin Masking

Johannes Reich, MSc, Institute of Physical and Theoretical Chemistry, University of Regensburg, Germany

Due to the fulminant physiological response endotoxin testing is mandatory in pharmaceutical production and product release of parenteral drugs. In order to solubilize certain active pharmaceutical ingredients, formulations contain surfactants (e.g. polysorbate) and buffer components (e.g. citrate), which can interact with endotoxin contaminations and prevent accurate detection (masking). We demonstrate that endotoxin masking depends on various parameters and provide dedicated approaches for a reliable detection of endotoxin contaminations.

12:00 pm Sponsored Presentations

(Opportunities Available)

12:30 Luncheon Presentation

(Sponsorship Opportunity Available)

1:15 Session Break

HIGH-THROUGHPUT SCREENING IN EARLY DEVELOPMENT

1:55 Chairperson's Remarks

Wayne F. Reed, Ph.D., Murchison Mallory Chair Professor of Physics, Department of Physics, Tulane University

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2:00 Alternative Methods for Quantifying Temperature- and Formulation-Dependent Aggregation Rates

Christopher J. Roberts, Associate Professor, Department of Chemical & Biomolecular Engineering, University of Delaware

Reliably predicting protein aggregation rates from accelerated storage conditions remains an outstanding challenge for formulation scientists. Issues that need to be overcome include: sufficiently accurate means to quantify how rates change with storage condition and non-linear effects that make extrapolations difficult to perform accurately. This talk presents illustrative methods to improve predictions of aggregation rates, with monoclonal antibodies as case studies, and also highlights remaining challenges for future efforts.

2:30 The Measurement of KD at Low Concentration and Its Application as a High-Throughput Screening Technique for Protein-Protein Interaction Measurements

Anthony L. Young, Ph.D., Principal Scientist, Pharmaceutical Research and Development, Pfizer

The light scattering measurement is routinely run in a high-throughput format to quickly determine the necessary diffusion coefficient versus concentration curves. The use of a robotic liquid handler can reduce the preparation time of the dilution sequence. This talk will cover the use of the liquid handler in combination with the dynamic light scattering instrument to generate KD values that are used to screen proteins and protein formulations for development. The data from several different protein isoforms will be discussed to illustrate the screening process and show typical data.

3:00 Simultaneous Stability and Aggregation Assessment by Isothermal Chemical Denaturation

Ernesto Freire, Ph.D., Professor, Biology and Biophysics, Johns Hopkins University

Stability and aggregation are two of the most important hurdles in the formulation of biologicals. Isothermal chemical denaturation (ICD) provides the most accurate way of measuring protein stability at room, physiological or storage temperatures under different solvent or formulation conditions, yielding reliable thermodynamic stability parameters. Furthermore, ICD experiments performed at different protein concentrations provide a quantitative assessment of protein aggregation in the native and denatured states. ICD is ideally suited to optimize the formulation of proteins hard to formulate, highly concentrated formulations, bispecific antibodies and antibody drug conjugates. In this presentation, the fundamentals of ICD and its application to the evaluation of protein stability and optimization of formulation conditions will be discussed.

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

4:15 Application of DSF as a High-Throughput Tool in Protein Characterization and Formulation Development

Shuai "Sunny" Shi, Ph.D., Senior Scientist, Sterile Product Development, Merck

In this study, we benchmarked DSF against the conventional thermal technique, differential scanning calorimetry (DSC), and more importantly made an attempt to predict protein thermal aggregation kinetics by DSF. We have defined three levels of correlations between DSF/DSC transition temperature and real-time thermal aggregation kinetics which will be shown in 3 individual case studies. We will also demonstrate the unique application of DSF in studying concentration-dependent thermal behaviors especially in the high-concentration range.

4:45 Increasing the Throughput of Protein Formulation Screening Using 96-Well Plate Format

Qingyan Hu, Scientist, Ph.D., Scientist, Formulation Development, Regeneron, Inc.

To increase throughput during formulation screening, the use of a 96-well plate format was explored for candidate selection and formulation development. Multiple mAb candidates were screened against different buffer/pH and excipients using the 96-well plate format. In addition, the stability study results obtained using the 96-well plate format was compared to the results from using glass vials. With the incorporations of an automated liquid handling system and analytical instruments compatible with 96-well plates, this approach would greatly increase the throughput of formulation screening and development.

5:15 End of Conference

5:15- 6:00 Dinner Short Course Registration

6:00 – 8:30 Dinner Short Course*: Accelerated Stability Testing of Biologics

*Separate registration required; see page 3 for details

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Early Analytical Development for Biotherapeutics

Optimizing the Selection and Performance of Preclinical Analytical Studies

STREAM 3
Analytical Development & Quality

Suggested Short Course*

Analytical Strategies for Comparability in Bioprocess Development

Tuesday, August 19, 6:00 – 8:30 pm

Separate registration required; see page 3 for details

WEDNESDAY, AUGUST 20

7:00 am Registration and Morning Coffee

BUILDING THE EARLY ANALYTICAL STRATEGY

8:05 Chairperson's Remarks

Vidyashankara Iyer, Ph.D., Scientist, Formulation Sciences, MedImmune

» 8:15 KEYNOTE PRESENTATION

Building a Robust Early Stage Analytical Characterization Process at the Discovery Research Stage

Laura Lin, Ph.D., Director, Biophysics, Analytics, & Bioconjugation, Biotherapeutics R&D, Pfizer

9:00 Application of a Simple and Fast Platform Method for DTPA in the Investigation of Co-Concentration of DTPA Due to the Donnan Effect during Processing of a Therapeutic mAb

Jason Huang, Ph.D., Senior Research Investigator, Analytical and Bioanalytical Development, Bristol-Myers Squibb

The chelating agent diethylene triamine pentaacetic acid (DTPA) is used in biologics formulations to prevent oxidation induced by metal ions and therefore improve protein stability. This presentation shows how a simple and fast platform method was applied for in-process monitoring of DTPA during biologics formulation development. The data obtained by this method demonstrated that there was a co-concentration of DTPA due to the Donnan effect during tangential flow filtration of a therapeutic mAb formulation.

9:30 Applying Inputs from Research Stage Studies and Developability Evaluations to the Early Analytical Strategy

Matthew Myers, Associate Scientist, Sterile Products Analytical Development, Merck

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

10:45 Development of an Early Analytical Strategy for a Novel Biotherapeutic

Patricia Lowden, Scientist, Protein Production and Analytics Department, Eleven Biotherapeutics

EBI-005 is a novel cytokine receptor antagonist for IL-1R and is currently in phase III development for dry eye disease. EBI-005 was characterized biochemically and biophysically at the earliest stages of development. Methods of characterization included CIEX- HPLC, RP-HPLC, SEC, SDS-PAGE, peptide mapping, DSF, CD and SIC. Extensive early characterization work has facilitated both purification process development, and formulation development. The extensive characterization has also led to constructive dialogue with regulators through the development stages.

11:15 Developability Evaluation for Novel Molecule Formats

Vidyashankara Iyer, Ph.D., Scientist, Formulation Sciences, MedImmune

11:45 Presentation Title to be Announced

Yan Wang, Ph.D., Scientist, Analytical Development, Biogen Idec

12:15 pm Luncheon Presentation

(Sponsorship Opportunity Available)

1:30 Session Break

HIGH-THROUGHPUT ANALYSIS IN EARLY DEVELOPMENT

1:55 Chairperson's Remarks

Jason Huang, Ph.D., Senior Research Investigator, Analytical and Bioanalytical Development, Bristol-Myers Squibb

2:00 High-Throughput Heterogeneity Analysis of Antibodies and Antibody-Like Molecules

Melissa Geddie, Ph.D., Senior Scientist, Merrimack Pharmaceuticals

Multispecific antibodies and antibody-like molecules broaden the therapeutic application of IgGs, but they can be challenging to engineer and manufacture. To address this we first use a network biology approach to identify key design parameters followed by iterative rational engineering, rapid design cycles and high-throughput screening assays to reduce heterogeneity. Our approach selects for potential therapeutic candidates with robust pharmaceutical properties.

2:30 Rapid Deployment of Analytical Methods during Early Stage Biologics Development

Marc Verhagen, Ph.D., Director, Biochemical Method Development, Allergan

Efficient support of process and formulation development activities during early stage programs require a variety of methods for monitoring key attributes of the compound of interest in samples with widely varying matrices. Approaches to establishing early stage methods, real time assessment of suitability for use for different sample types, and handling of documentation associated with the initial stages of the method lifecycle will be discussed.

3:00 Efficient Evaluation of Product Quality Attributes during Early Development

Pete Vandeberg, Ph.D., Director, Analytical Development, Grifols

During early phase development, prioritization is placed on methods needed to support process development and pre-clinical studies. Focus is generally placed on methods to measure activity and purity. Methods should have quick turn around times and low manpower requirements. Analytical characterization data gathered should be positioned to file the IND and aid in further development.

3:30 Refreshment Break

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4:15 High-Throughput Analytical Platforms to Assess Product Quality Attributes at Early Stage of Cell-Line Development

Shashi Prajapati, Ph.D, Senior Scientist, Biogen Idec

Here we present high-throughput (HTP) analytical assays to facilitate rapid product quality using 96-well plate formats. These HTP product quality assays include HTP protein quantitation followed by HTP protein purification and product quality analyses. With these HTP analytical product quality assays, we can assess product quality in the early stage of clone screening, as well as expedite the cell-line and process development.

4:45 Automation of Bioanalytical Ligand-Binding Assays Using Modular Robotic Scripts as a Generic Template in Support of Discovery Biotherapeutic Programs

Jia Duo, Ph.D., Research Investigator, Analytical and Bioanalytical Development, Bristol-Myers Squibb

Traditional automation-assisted ligand-binding assays (LBAs) use assay-specific scripts requiring labor-intensive script writing and user training. Major nonspecific script modules were developed to facilitate automated sample preparation and LBA procedures. The modular design of general automation scripts allows users to assemble automated assays with minimal script modification. Results demonstrate that the modular scripts provide flexibility in adapting to various LBA formats and significant time savings in script writing and scientist training.

5:15 Networking Reception in the Exhibit Hall with Poster Viewing

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6:30 End of Day

THURSDAY, AUGUST 21

8:00 am Registration and Morning Coffee

EARLY DEVELOPMENT ASSAYS

8:25 Chairperson's Remarks

Vijay Dhawan, Ph.D., Scientist, Bioanalytical Development, Genzyme

8:30 Insights from Recent Regulatory Filings and Pre-IND Meetings with FDA

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

9:00 Streamlining Antibody Characterization by Simultaneously Monitoring Multiple Product Quality Attributes

Catherine Eakin, Ph.D., Senior Scientist, Amgen

Process control of biopharmaceuticals is critical for ensuring product quality, safety and efficacy for patients. Owing to their complexity, large molecules inherently have heterogeneity; however, throughout development multiple analytics are employed to define process consistency. We utilize a single mass spectrometry based method that can simultaneously measure multiple individual product quality attributes. This approach is more efficient than conventional characterization strategies and provides product characterization at the residue specific level.

9:30 Analytical Characterization of Inline claMP Tag Protein-Metal Conjugates

Jennifer S. Laurence, Ph.D., Associate Professor, Pharmaceutical Chemistry, University of Kansas

Metals are central components of imaging diagnostics, chemotherapeutics, and biotechnology reagents. Synthetic chelators are used to bind metals and are chemically conjugated to proteins for targeted applications. Metal-binding peptide tags offer a linker-less alternative. Both approaches are much more effective with lanthanides than transition metals. We developed the metal abstraction peptide (MAP) chemistry and engineered the linker-less claMP Tag to enable usage of more biocompatible metals. Characterization of these inline conjugates will be presented.

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

10:45 Key Quality Attributes during the Early Stage Development of a Biologic – What Is Important for this Stage of the Program?

Vijay Dhawan, Ph.D., Senior Scientist, Bioanalytical Development, Genzyme

During the early stage development of a biologic, selective preliminary critical quality attributes (CQAs) should drive the initial analytical characterization of the molecule. It is of paramount importance that these efforts focus on attributes with a possible linkage to the clinical outcome. Biological activity, identity and purity are examples of few such attributes. The analytical efforts to characterize these attributes can serve a longstanding purpose during the lifecycle management of the molecule. The choice of these attributes and the associated analytical tools will be discussed.

11:15 Generic vs. Specific Immunoassays for Quantification of Biotherapeutics in Late Research and Early Development

Kelly Loyet, Ph.D., Scientist, Biochemical and Cellular Pharmacology, Research, Genentech

It is necessary to evaluate potential biotherapeutics with preclinical pharmacokinetic (PK) assays. These assays measure the concentration of biotherapeutics in a biological matrix. Commonly, quantitative immunoassays are developed with analyte-specific reagents, although it is also feasible to use a generic approach with reagents that could quantify any biotherapeutic in its class. These strategies may also be complementary to further explore or confirm unexpected results.

11:45 The Roles of Analytical Development and Protein Characterization in Late Stage Discovery Research and Early Stage Development

Andrew Downey, Ph.D., Researcher, Chemistry, University of Massachusetts Lowell

Analytical methods examining the critical structural and functional aspects of protein products should be established by late stage discovery research and early stage product development. Examples of analytical studies discussed include characterization of structural isoforms, assessment of functionality and identification of degradation pathways, with a focus on evaluation of 'manufacturability.' Though encompassing various factors, early recognition of drawbacks to effective protein manufacturing ultimately contributes to product quality and economy of development.

12:15 pm Sponsored Presentation

(Opportunity Available)

12:30 Sponsored Luncheon Presentation

(Opportunity Available)

1:15 End of Conference

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3rd Annual

Higher-Order Protein Structure

Characterization, Prediction, Comparability and Biosimilars

STREAM 3
Analytical Development & Quality

Suggested Short Course*

Biophysical Characterization in Developing Biopharmaceuticals: The Path to Developability, Stability and Comparability

Thursday, August 21, 6:30-9:30 pm

Separate registration required; see page 3 for details

THURSDAY, AUGUST 21

HIGHER-ORDER PROTEIN STRUCTURE: MECHANISM AND IMPACT

1:55 pm Chairperson's Remarks

Yatin R. Gokarn, Ph.D., Narotam Sekhsaria Distinguished Professor of Chemical Engineering, Institute of Chemical Technology, Mumbai, India

» 2:00 KEYNOTE PRESENTATION

Characterization of Protein Higher Order Structure in Comparability & Biosimilarity: A Regulatory Perspective

Maria-Teresa Gutierrez-Lugo, Ph.D., Product Quality Reviewer, Division of Therapeutic Proteins, OBP/Center for Drug Evaluation and Research, US Food and Drug Administration

Protein Higher Order Structure (HOS) plays a critical role in a product's activity and stability. Differences in protein HOS between a reference product and a proposed biosimilar product have the potential to impact product performance. This presentation will provide an overview of the regulatory expectations for analytical similarity with a focus on the evaluation of HOS. Challenges related to an assessment of HOS using current methodologies will be also discussed.

2:45 Measuring Higher-Order Structure of Proteins: Rationale, Methodologies and Expected Outcomes

Yatin R. Gokarn, Ph.D., Narotam Sekhsaria Distinguished Professor of Chemical Engineering, Institute of Chemical Technology, Mumbai, India

Subtle changes in the complex 3-D structures of protein-based drugs can have profound effects on efficacy and safety. Therefore the HOS of protein-drugs needs to be carefully analyzed and tracked through various stages of development, and product cycle. We present an approach that combines analyses of global solution state and behavior along with signatures of secondary and tertiary structure using orthogonal biophysical techniques. We show that a consistent, information-rich HOS map can be created for a given molecule, which can be helpful towards establishing analytical comparability.

3:15 Understanding the Importance of Local Structure for Protein Stability

Jennifer S. Laurence, Ph.D., Associate Professor, Department of Pharmaceutical Chemistry, University of Kansas

Stability depends on both protein composition and the solution environment into which it is placed. Standard approaches to examining protein stability rely on global measures of structure or aggregation of the product. These low-resolution techniques facilitate rapid identification of compatible conditions, but insight about how stabilization is achieved has remained elusive. Solution NMR was used to detect changes to individual residues, and specific influences on stability were extracted from cross-correlation with standard evaluation methods to assess mechanisms of instability in proteins.

3:45 Sponsored Presentation *(Opportunity Available)*

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

ANALYTICAL COMPARABILITY AND BIOSIMILARITY

4:45 Assessing Aggregate Content in Originator Products as a Specification Guideline for Biosimilars

Christina R. Vessely, Ph.D., Director CMC & Regulatory Affairs, KBI Biopharma

Setting specifications for aggregate content in early clinical stages for a biotechnology product can be challenging due to limitations of analytical methods and limited experience in the clinic. In the case of biosimilars, the specification must also consider aggregate levels in the originator product. This presents an additional challenge because biosimilar companies typically don't have access to true T=0 originator material. This presentation discusses strategy for setting an appropriate aggregate specification for a biosimilar product.

5:15 A Unique High-Throughput Assay for Determination of the Comparability of the Potency and Neutralizing Antibody Response to Biosimilars and Innovator Products

Michael G. Tovey, Ph.D., INSERM Director, Research, Laboratory of Biotechnology and Applied Pharmacology, ENS-Cachan, France

Successful development of biosimilars is dependent upon the establishment of validated and standardized assays that allow direct comparisons of the relative potency and immunogenicity of innovator molecules and biosimilars. A validated standardized high-throughput cell-based assay platform will be described that is applicable to most biopharmaceuticals and that allows the direct comparison of drug potency and anti-drug neutralizing antibody responseof innovator molecules and biosimilarsin the same assay.

5:45 End of Day

5:45 – 6:30 Dinner Short Course Registration

6:30 – 9:00 Dinner Short Course*: Biophysical Characterization in Developing Biopharmaceuticals: The Path to Developability, Stability and Comparability

Separate registration required; see page 3 for details

FRIDAY, AUGUST 22

8:00 am Registration and Morning Coffee

HIGH-RESOLUTION COMPARABILITY TOOLS

8:25 Chairperson's Remarks

Jennifer S. Laurence, Ph.D., Associate Professor, Department of Pharmaceutical Chemistry, University of Kansas

8:30 Qualification of Analytical Method Used for Characterization of Protein Higher Order Structure

Marina Kirkitadze, Ph.D., Deputy Director, Analytical Research & Development, Sanofi Pasteur, Canada

The topic of this presentation is qualification of an analytical method. Qualification consists of a simplified

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evaluation of a subset of validation characteristics. There are no predefined acceptability criteria for evaluation of qualification characteristics, and the purpose to collect experimental data to demonstrate whether an analytical method is suitable for its intended use. Qualification of Differential Scanning Calorimetry (DSC) is shown as an example.

9:00 NMR Fingerprinting the Higher-Order Structure of Biosimilars: A High Resolution Comparability Tool

Yves Aubin, Ph.D., Research Scientist, Protein Structure and Analysis Laboratories, Regulatory Research Division, Centre for Biologics Evaluation, Health Canada

Filgrastim is the generic name for recombinant methionyl human granulocyte colony-stimulating factor (r-metHuG-CSF). It is used for the treatment of neutropenia and it is marketed under the brand name Neupogen® by Amgen. Here we show that a simple NMR fingerprint assay can be used to assess the three-dimensional structure of the active ingredient in the formulated product at high-resolution. In addition, the results of an inter-laboratory NMR study of Neupogen® and biosimilars from the market place will be presented to demonstrate the robustness and precision of the method.

9:30 Adopting Imaging and Other Techniques to Study Novel Therapeutic Modes Such as the DVD-IgTM Molecule

Ivan R. Correia, MBA, Ph.D., Senior Principal Research Scientist, Protein Analytics, Process Sciences, AbbVie Bioresearch Center

The architecture and dynamics of a DVD-Ig™ molecule and its parental mAbs was examined using single particle electron microscopy. Hinge angles measured for the DVD-Ig™ molecule were similar to the inner antigen parental mAb. The outer binding domain of the DVD-Ig™ molecule was highly mobile and three-dimensional (3D) analysis showed binding of inner antigen caused the outer domain to fold out of the plane with a major morphological change. Docking high-resolution X-ray structures into 3D electron microscopy map supports the extraordinary domain flexibility observed in the DVD-Ig™ molecule allowing antigen binding with minimal steric hindrance.

10:00 Mid-Morning Snack in the Exhibit Hall with Poster Viewing

10:45 Application of High Resolution UPLC-MS in Drug Product Comparability Studies

Yimin Hua, Ph.D., Quality Control Scientist I, Genzyme Corporation, a Sanofi Company

The comparability study will involve not only demonstration of analytical equivalence for protein structures, it also verify that the products have similar quality attributes and equivalent functionality. The product biological activities as well as safety are examined, including host cell DNA and proteins, degradants, aggregates of proteins, etc. The analytical demonstration in similarity commonly involves the use of forced degradation methods such that both structure quality attributes as well as product degradation pathways are also compared. This talk will present comparability studies utilizing the state-of-the-art technology with high resolution UPLC-MS technique

11:15 Advanced Mass Spectrometry for the Characterization of Biopharmaceutical Post-Translational Modifications

Angelo Palmese, Ph.D., Junior Researcher, Structural Characterization, Analytical Development Biotech Products, Merck Serono (Italy)

A detailed knowledge of the protein structure is a prerequisite for the development of biopharmaceuticals. The conformation of a protein determines its function and is largely defined through its primary structure, although it can also be significantly influenced by post-translational modifications (PTMs). In this talk, a case study will be presented in which the intact molecule analysis, by means of mass spectrometry techniques, allowed explaining differences in CDC (Complement-dependent Cytotoxicity) among samples manufactured by two different processes.

11:45 Characterization of the NIST Standard Monoclonal Antibody by 2D NMR Fingerprinting Methodologies

Robert G. Brinson, Ph.D., NIST Research Chemist, Institute for Bioscience & Biotechnology Research, University of Maryland Baltimore

The development of advanced techniques, such as NMR spectroscopy, for the characterization of tertiary and higher order structure in protein therapeutics is emerging as a major priority in the pharmaceutical industry. To demonstrate the viability and applicability of NMR fingerprinting techniques, we have examined the IgG-based NIST standard monoclonal antibody and present its NMR amide and methyl fingerprint. We further demonstrate rapid acquisition techniques to afford a CH-methyl spectral fingerprint in less than one hour.

12:15 pm Site Directed Spin Labeling to Assess Higher Order Protein Structure

David E. Budil Ph.D., Associate Professor of Chemistry and Chemical Biology; Associate Dean for Research, College of Science, Northeastern University

The spin label method, combined with site-directed Cys substitutions in proteins, has been shown to be of immense utility to protein structure determination where other methods fail. This methodology is highly suited for membrane proteins as crystallographic methods are often not possible in such cases. The advantages are no requirement for optical transparency, molecular weight limits are not an issue, and measurements can be carried out in the solid state.

12:45 Luncheon Presentation *(Sponsorship Opportunity Available)*

TOOLS & METHODS FOR HOS CHARACTERIZATION

1:25 Chairperson's Remarks

Marina Kirkitadze, Ph.D., Deputy Director, Analytical Research & Development, Sanofi Pasteur, Canada

1:30 Advantages of Hydrogen Deuterium Exchange Mass Spectrometry in Understanding Multi-Domain Proteins

Thomas E. Wales, Ph.D., Research Assistant Professor, Department of Chemistry and Chemical Biology, The Barnett Institute of Chemical and Biological Analysis, Northeastern University

Intramolecular interactions in multi-domain proteins may play a major role in protein function. Hydrogen deuterium exchange mass spectrometry (HDX MS) can be used to investigate how domains influence one another, and in particular how domain interactions can influence activity from a distance. The application of HDX MS for this purpose will be described for several proteins of varying size and domain architecture.

2:00 Evaluation of Vibrational Spectroscopic Techniques for Structural Characterization of a Therapeutic Monoclonal Antibody in Formulation Matrix

Geetha Thiagarajan, Ph.D., Senior Scientist, Sterile Product and Analytical Development, Merck & Co.

Structural complexity of biological drug products presents an analytical challenge in terms of early detection of aggregation and/or degradation. A set of

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Characterization, Prediction, Comparability and Biosimilars

STREAM 3
Analytical Development & Quality

spectroscopic and non-spectroscopic analytical tests (HP-SEC, SV-AUC, Raman, ROA, CD, Fluorescence, FTIR and DLS) were evaluated for their sensitivity to detect heat-induced molecular instability in a therapeutic monoclonal antibody present in its formulation matrix. The first signs of biophysical changes in the molecule were degradation involving exposure of hydrophobic patches due to partial unfolding, followed by aggregation. Sensitivity of the different assays was rank ordered.

2:30 Probing Higher-Order Structure in Protein Pharmaceuticals Using Infrared and Raman Vibrational Optical Activity

Laurence A. Nafie, Ph.D., Distinguished Professor Emeritus, Department of Chemistry, Syracuse University

Vibrational optical activity (VOA), comprised of infrared vibrational circular dichroism (VCD) and vibrational Raman optical activity (ROA) provides enhanced sensitivity to higher order structure (HOS) in proteins compared to their parent IR and Raman spectra, as well as other spectroscopic techniques. Examples of the sensitivity of VOA to both protein secondary structure and HOS in proteins will be presented as a sensitive new tool for evaluating structural differences between originator biopharmaceuticals and their bio-similars.

3:00 Refreshment Break

3:15 Comparison of Higher Order Structure of Soluble and Insoluble Protein

Kelly Neelon, Ph.D., Associate Director, Drug Product Formulation, Momenta Pharmaceuticals, Inc.

Characterization of higher order structure can be instrumental in determining the sensitivities of a molecule to processing conditions during manufacturing. This talk will discuss utilization of chemical and biophysical techniques to compare the higher order structure of a protein in the soluble and insoluble state and feedback of this information to improve processing conditions.

3:45 Applications of Hydrogen Deuterium Exchange – Mass Spectrometry for Biopharmaceutical Development

Damian Houde, Ph.D., Scientist II, Protein Pharmaceutical Development, Biogen Idec; Adjunct Professor, Northeastern University

Protein biopharmaceuticals can exhibit unwanted properties when solution conditions are changed. Analytical tools capable of detecting changes in a protein rapidly, accurately, and with high sensitivity are therefore highly desirable to the biopharmaceutical industry. Hydrogen/deuterium exchange mass spectrometry (H/DX-MS) can be useful for investigating protein conformation, dynamics and interactions. In this presentation, specific applications of H/DX-MS will be discussed that include the characterization of protein biopharmaceuticals at high concentrations.

4:15 End of Conference

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CMC Strategies for Antibody-Drug Conjugates

Linking Process, Methods and Assays for the Manufacture of ADCs

STREAM 4
Development of Next-Generation Biologics

Suggested Short Course*

ADC "Developability": Critical Quality Attributes Inform Formulation and Process Development

Monday, August 18, 9:00 – 11:30 am

*Separate registration required; see page 3 for details

MONDAY, AUGUST 18

8:00 am Pre-Conference Registration and Morning Coffee

9:00 – 11:30 Short Course:* ADC "Developability:" Critical Quality Attributes Inform Formulation and Process Development

*Separate registration required; see page 3 for details

11:30 Main Conference Registration

1:00 pm Chairperson's Opening Remarks

Janet L. Wolfe, Ph.D., President, Wolfe Laboratories

» KEYNOTE PRESENTATIONS

1:10 Innovations, Challenges and Opportunities in Antibody-Drug Conjugates

Janet L. Wolfe, Ph.D., President, Wolfe Laboratories

Antibody-drug conjugates (ADCs) are a rapidly growing therapeutic class that leverages the targeting specificity of antibodies with the potency of small molecules. These highly complex molecules require synchronized tuning of multiple components, creating large technical challenges. Excitement within this burgeoning field is causing enormous innovation around various ADC formats, creating even greater technical barriers. An overview of the field will be provided, with a focus on the challenges and opportunities of well defined CMC strategies.

1:45 Druggable Extracellular Targets

James Prudent, Ph.D., President & CEO, Centrose

The rate limiting internalization step for ADCs requires extremely toxic drugs. If there were external drug targets that could be mined, antibody conjugates would not require internalization and less toxic drugs could be employed. This talk discusses potential targets that rest on the outside of the cell and show data on how such extracellular drug conjugates can be used for numerous indications. The talk will also review some of the development and CMC benefits that extracellular drug conjugates bring.

BIOCONJUGATION ENABLING DEVELOPABILITY AND MANUFACTURABILITY OF ADCs

2:15 Generation of ADCs 2.0 Using Novel Toxins and Site-Specific Coupling

Andreas Pahl, Ph.D., CSO, Heidelberg Pharma

Toxic warheads of today's ADCs are exclusively based on compounds acting on microtubules or DNA replication and seem to suffer from limitations in certain cancer indications and tumor cells. New generations of payloads enter the field including Heidelberg Pharma's amanitin, a highly effective inhibitor of the eukaryotic RNA Polymerase II. Site specific conjugation is going to overcome some these limitations. This presentation will summarize the current status of new toxins and appropriate conjugation methods.

2:45 Refreshment Break

3:15 Carbohydrate-Mediated Site-Specific Antibody-Drug Conjugation

Qun Zhou, Ph.D., Principal Scientist, Protein Engineering, Genzyme, a Sanofi Company

Multiple antibody-drug conjugates have been approved recently. However, the classical chemistries to produce these conjugates by targeting primary amines and disulfides have some shortcomings including heterogeneous product profiles. We have developed a novel site-directed conjugation strategy targeting native carbohydrates of proteins to improve the anti-tumor efficacy of antibody-toxin conjugate. Our method provides a viable alternative without re-engineering of protein sequences.

3:45 Optimizing ADC Properties through Site-Specific Conjugation

Nick Knudsen, MSc., Group Leader, Purification and Bioconjugate Development, Ambrx, Inc.

Antibody-drug conjugates, or ADC, combine high potency payloads with the targeting specificity of antibodies. They hold tremendous potential in the treatment of cancer but are also emerging as therapeutic agents outside of oncology. Unfortunately, ADC have also been historically complex to manufacture and characterize due to the use of non-specific conjugation chemistry. Here, we present data on using site specific conjugation to improve the attributes of ADC and improve their chance of success during development.

4:15 Breakout Discussions

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. Then continue the discussion as you head into the lively exhibit hall for information about the latest technologies.

5:15 Discussion Report-Outs

5:30 Grand Opening Reception in the Exhibit Hall with Poster Viewing

7:00 End of Day

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CMC Strategies for Antibody-Drug Conjugates

Linking Process, Methods and Assays for the Manufacture of ADCs

STREAM 4
Development of Next-Generation Biologics

TUESDAY, AUGUST 19

7:30 am Registration and Morning Coffee

ANALYTICAL CHARACTERIZATION AND FORMULATION

7:55 Chairperson's Remarks

8:00 The Heterogeneity of ADCs and Its Impact on Analytical Method Development and Characterization

Lily Liu, BS, Principal Associate, Formulation and Analytical Development, Agensys, Inc.

The possible combinations of payloads and IgG isotypes confer additional heterogeneity to the ADC molecules, adding an extra layer of complexity over their mAb counterparts. This presentation will focus on challenges with regards to analytical methods and our approach to develop fit-for-purpose methods for release and stability testing to support IND filings. Characterization of the methods and the inferences to the structure of the ADCs will also be discussed.

8:30 Photodegradation Reactions of Antibodies and Antibody-Drug Conjugates

Christian Schöneich, Ph.D., Takeru Higuchi Distinguished Professor and Chair, Pharmaceutical Chemistry, University of Kansas

Chemical and physical stability problems of ADCs may arise from the exposure of ADCs to light, as (i) several ADCs contain drug conjugates, which may act as photosensitizer (e.g., CBI, duocarmycin or an anthraquinone moiety), and/or (ii) the conjugation of drug moieties to antibodies may change the sensitivity towards light exposure. This talk will focus on light-induced photodegradation of ADC mimics, designed to evaluate the light-sensitivity and degradation mechanisms of ADCs.

9:00 Characterization of Conformational Stability of Antibody-Drug Conjugates

Prasanta Patel, Ph.D., Principal Scientist, Progenics Pharmaceuticals

Conformational stability of an antibody-drug conjugate relies on the structural integrity of the molecule. Elucidation of conformational aspects of the antibody is complex therefore orthogonal methods are frequently applied. Conformational stability of an antibody with a cytotoxic payload may alter the binding properties and potency of the conjugated antibody. An overview of various analytical methods for characterization of conformational stability of the antibody-drug conjugate will be presented.

9:30 Sponsored Presentation
(Opportunity Available)

9:45 Coffee Break in the Exhibit Hall with Poster Viewing

10:30 The Role of High Drug Payload on Physical Instability of Antibody-Drug Conjugates

Yilma Adem, MSc, Formulation Scientist, Pharmaceutical Development, Genentech, Inc.

11:00 CQA-Based Approaches to Formulation Development of an ADC Program

Aditya Wakankar, Ph.D., Associate Director, Formulation & Analytical Development, Stem CentRx LLC.

Knowledge of CQA for ADCs is being incorporated into the design of safe, efficacious and stable ADC drug product formulations. Quality attributes for an ADC can be categorized into those that are associated with the antibody-drug conjugate, the drug itself and those that are inherited from the antibody intermediate. This talk will provide perspective on what attributes are critical for an ADC (e.g. DAR, free drug) and how this information can be utilized to make informed formulation plans and decisions.

11:30 Development and Comparative Stability of Liquid and Lyophilized Formulations for a Developmental Maytansinoid ADC

Karan Shah, MSc., Analytical Associate III, Analytical and Pharmaceutical Sciences, Immunogen, Inc.

This presentation will discuss the screening studies that were performed to develop viable liquid and lyophilized formulation candidates for a development stage maytansinoid ADC. The stability of the candidate formulations will be compared using a variety of analytical methods including SE-HPLC, RP-HPLC and reduced/non-reduced CE SDS. Important differences in the requirements for developing liquid and lyophilized formulations will also be discussed.

12:00 pm Sponsored Presentations
(Opportunities Available)

12:30 Luncheon Presentation
(Sponsorship Opportunity Available)

1:15 Session Break

CMC, PROCESS DEVELOPMENT AND REGULATORY CONSIDERATIONS

1:55 Chairperson's Remarks

Ian Schwartz, MSc., Senior Engineer, Process Development, Agensys, Inc.

2:00 Regulatory CMC Considerations for ADC Clinical Development

Mark Tardie, MSc., Senior Regulatory Manager, Global Biotherapeutics CMC, Pfizer, Inc.

The significant number of antibody-drug conjugates (ADCs) currently in development is testament to their promising therapeutic benefit. In addition to the complexity of unconjugated monoclonal antibodies, ADCs exhibit unique properties, derived from the linkage of a biologically produced antibody to a small molecule drug, which require careful CMC consideration. This presentation will explore ADC development challenges, including the current lack of comprehensive specific regulatory guidance, the use of highly potent cytotoxic agents and the need for heightened analytical testing.

2:30 Process Development of Scalable Antibody-Drug Conjugate Manufacturing Processes: Points to Consider and Parameters to Control

Ian Schwartz, MSc., Senior Engineer, Process Development, Agensys, Inc.

Antibody-Drug Conjugates (ADCs) are an exciting class of targeted therapies for the treatment of cancer. ADCs have process development and manufacturing challenges in part due to the uniqueness of combining a tumor targeting antibody with a potent small molecule cytotoxic

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STREAM 4
Development of Next-Generation Biologics

agent. This presentation gives strategies for process development of scalable and robust ADC manufacturing processes.

3:00 Challenges and Considerations for Clinical Development and Manufacturing of ADCs

Steven Max, Ph.D., Associate Research Fellow, Biotherapeutics Pharmaceutical Sciences, Pfizer, Inc.

The increased interest in antibody-drug conjugates (ADCs) is a testament to their potential therapeutic and safety advantages over conventional chemotherapies. The ADC toolbox enables, for example, the ability to evaluate different linker-payload combinations, drug load (DAR) and conjugation chemistries in order to optimize stability, safety and efficacy in the clinic. However, these same options can provide CMC-specific challenges en route to regulatory approval and clinical dosing. This talk will address some key considerations during the development and manufacturing of ADCs.

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

4:15 Externalization of ADC Manufacturing: Challenges and Triumphs

Vincent Turula, Ph.D., MBA, Director, Biotherapeutics Pharmaceutical Sciences, Pfizer, Inc.

The manufacture of Antibody-Drug Conjugate clinical trial material is complex as it involves the rapid assembly of many components across a network of specialized service providers. Regardless of the stage of development, from clinical to commercial, production and testing must be coordinated and integrated into robust work streams. The focus of this presentation will be on the challenges that exist in outsourcing ADC manufacture and how a sound strategy and operational consistency can lead to shorten timelines and reduced cost.

4:45 Challenges in ADC Process Development and Scale Up

Xavier Despinoy, Ph.D., Process Development Manager, Piramal Healthcare Ltd.

The presentation will focus on two standard ADC conjugation processes - partial reduction and lysine chemistries. Following general process development and scale-up considerations, parameters affecting the reactive stages will be reviewed. Development of TFF purification stage and consideration for chromatography will also be discussed.

5:15 End of Conference

5:15- 6:00 Dinner Short Course Registration

6:00 – 8:30 Dinner Short Course*: Analytical Strategies for Comparability in Bioprocess Development

Separate registration required; see page 3 for details

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Process Development for Novel Biotherapeutic Formats

STREAM 4
Development of Next-Generation Biologics

Suggested Short Course*

Analytical Strategies for Comparability in Bioprocess Development

Tuesday, August 19, 6:00 – 8:30 pm

Separate registration required; see page 3 for details

WEDNESDAY, AUGUST 20

7:00 am Registration and Morning Coffee

PROCESS DEVELOPMENT FOR NOVEL MOLECULES

8:05 Chairperson's Remarks
Amardeep Bhalla, Ph.D., Principal Scientist, Pfizer

» 8:15 KEYNOTE PRESENTATION
Process Development in an Era of New Product Formats and Changing Technologies
Steven Lang, Ph.D., MBA, Scientific Director, Biologics Research, J&J Biotechnology Center of Excellence
The biotechnology industry has created huge advances in efficiencies through the adoption of platform processes during the last 10 years. New therapeutic formats and technologies will challenge platform processes and many development organizations. Success in the next years will depend on creating intelligent flexibility in multiple platform development processes.

9:00 Rapid Characterization of Recombinant Protein's CQAs: HMW Species and Particulates Determination Using Novel Technologies at Line during Product Process Development Lifecycle
Nesredin Mussa, Ph.D., Global Manufacturing and Supply, Bristol-Myers Squibb

9:30 Case Studies of Early Process Development for Multi-Component Vaccines
Amardeep Bhalla, Ph.D., Principal Scientist, Pfizer

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

10:45 Case Study: Development and Manufacturing of a Common Light Chain Bispecific Antibody: MCLA-128
Lex Bakker, Ph.D., Chief Development Officer, Merus, The Netherlands
MCLA-128 is an ADCC-enhanced human common light chain bispecific IgG1 antibody targeting HER2 and HER3. MCLA-128 demonstrates potent inhibition of HER2:HER3 heterodimer signaling and robust anti-tumor activity in a trastuzumab-resistant xenograft model. It is produced in CHO cells using low fucose expression technology and Merus' proprietary CH3 engineering to force bispecific IgG heterodimerization. A robust purification process was developed resulting in ultra pure MCLA-128 at high process yields. MCLA-128 is currently undergoing cGMP manufacturing to allow clinical evaluation in a planned first-in-human phase I study.

11:15 Challenges and Insights in Rapid Process Development for Insourced Biotherapeutics of Varying Formats: A Case Study in Upstream Strategy
Brian Doyle, Senior Research Associate, Gilead

11:45 High-Throughput Screening of Single Cells Using Droplet Microfluidics
Linas Mazutis, Ph.D., Visiting Scholar, School of Engineering & Applied Sciences, Harvard University

12:15 pm Luncheon Presentation
(Sponsorship Opportunity Available)

1:30 Session Break

CASE STUDIES OF UPSTREAM PROCESSING

1:55 Chairperson's Remarks
Pratik Jaluria, Ph.D., Associate Director, Alexion Pharmaceuticals

2:00 Upstream Process Development for DARTs: Challenges and Opportunities with Novel Antibody-Like Bispecifics
Andrew Snowden, Ph.D., Director, Cell Culture Sciences, Macrogenics, Inc.
DART (Dual Affinity Re-Targeting) molecules are highly modular antibody-like therapeutic proteins in development for the treatment of human diseases in the oncology, antiviral and autoimmune related therapeutic areas. Data will be presented showing that unlike a number of bispecific formats, DARTs possess superior molecular attributes that facilitate the routine development of high-titer processes. Examples will be presented including aspects of CHO production cell line generation and the development of high-titer upstream bioprocesses for this new class of antibody-like bispecifics.

2:30 Cell Culture Process Development for a Novel Bispecific Antibody
Benjamin Wang, Ph.D., Senior Bioprocess Engineer, Merrimack Pharmaceuticals

3:00 Collaboration between Upstream and Downstream to Resolve the Challenges of a Novel, Difficult-to-Express Protein
Alan Gilbert, Ph.D., Senior Engineer, Cell Culture Development, Biogen Idec
An upstream process was designed to increase titer of a small, but highly positively charged protein. One of the unique challenges with this particular protein was the protein's adherence to the cell surface. A critical step was identifying a new feed medium additive to increase titer that ultimately interfered with the ability to purify the protein. Extensive collaboration between upstream and downstream was required as a result, and integrating this development debottlenecked the process.

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

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Process Development for Novel Biotherapeutic Formats

STREAM 4
Development of Next-Generation Biologics

4:15 Antibody Cocktails: Resolving Batch-to-Batch Variation and Cell Line Stability

Hugh H. Russell, Ph.D., Director, Antibody Technologies, Excelimmune

Manufacturing of Antibody Combination Therapeutics (ACTs) requires reproducible antibody stoichiometry during production. The presentation will discuss production of cell lines vs. stable pools and methods of cell line creation. Research demonstrates AAV-based integration is superior to random integration for cell line generation and that stable pools are capable of maintaining a consistent antibody ratio during culture.

4:45 Improve-Ization: Challenges in Re-Development of a Late-Stage Upstream Process

Pratik Jaluria, Ph.D., Associate Director, Alexion Pharmaceuticals

In developing a new, more productive upstream process for a late-stage therapeutic protein, a number of challenges were encountered. This presentation describes experimental work across multiple scales evaluating process changes designed to retain key product quality metrics while overcoming the limitations in our existing cell culture platform process.

5:15 Networking Reception in the Exhibit Hall with Poster Viewing

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6:30 End of Day

THURSDAY, AUGUST 21

8:00 am Registration and Morning Coffee

CASE STUDIES OF DOWNSTREAM PROCESSING

8:25 Chairperson's Remarks

Amith Naik, Ph.D., RAC, Senior Scientist, Biomanufacturing Training and Education Center, North Carolina State University

8:30 Process Development Challenges for FGF21 Protein-Antibody Conjugates

Rory Finn, Principal Scientist, Conjugate and Polytide Process Development, Biotherapeutics Pharmaceutical Sciences, Pfizer

One strategy for improving the pharmacokinetics and potency of peptides, proteins or other bioactive molecules is through conjugation to antibody scaffolds engineered with specific attachment sites. The complexity of such molecules presents unique challenges for developing processes viable for clinical and commercial manufacturing. This presentation will focus on the pilot scale process development optimization for two protein-antibody clinical candidates: 1) a FGF21 analog protein– antibody conjugate, and 2) an asymmetric bi-functional antibody conjugate containing one FGF21 analog protein and one GLP-1 mimetic peptide. Strategies directed toward reducing material consumption, shortening process times, and increasing yields will be discussed.

9:00 Purification Challenges for High-Concentration Monoclonal Antibodies

Hong Li, Ph.D., Principal Scientist, Purification Process Development, Merck

Developing a successful high-concentration formulation of monoclonal antibody for subcutaneous delivery is increasingly desirable. Solubility of the target protein, opalescence, viscosity, and aggregation can result in significant challenges for the manufacturing process. This presentation will focus on the challenges during the development of an Ultrafiltration (UF) step. Developability assessment for target proteins, membrane type system set up for high recovery, and process scale-up are highlighted for discussion.

9:30 Impact of Inclusion Body Quality on Downstream Processing of Novel Biotherapeutic Molecules

Timothy Pabst, Ph.D., Scientist, Purification Process Science, MedImmune

Refolding of proteins with acceptable yield for the production of therapeutic drug products remains a challenge and requires high quality inclusion bodies. We present an informative case study on the impact of inclusion body quality on product yield and quality by comparing a clinical manufacturing process for a recombinant immunotoxin with the commercial process that was developed to replace it. A systematic approach to commercial process development led to five-fold increase in yield and eliminated fractionation and in-process testing.

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

10:45 Downstream Process for Single Chain Antibody Fragment

Amith Naik, Ph.D., RAC, Senior Scientist, Biomanufacturing Training and Education Center, North Carolina State University

Antibody fragment-based drugs have the high specificity of whole antibody but offer better tissue penetration and less immunogenicity. However, the lack of the Fc region means that the Protein A based platform purification process cannot be employed for antibody-fragments. We present the development of a downstream process for capture and purification of an scFv from bacteria (*E. coli*) lysate and yeast supernatant. The process comprising of two steps, diafiltration and ion exchange chromatography purified scFv with a purity and recovery of 97% and 90% respectively.

11:15 Enabling Industrial Production of Lentiviral Vectors for Gene Therapy

Michael Kuczewski, Ph.D., Scientist, Purification Process Development, Bluebird Bio

With the approval of the first gene therapy product in the EU and a growing number of advanced clinical trials ongoing, this class of biotherapeutics is finally reaching maturity. Lentiviral vectors are an ideal platform for indications requiring long-term, stable expression, but the production processes have historically not been scalable. While many techniques can be borrowed from the world of protein therapeutics, the nature of lentiviral particles poses significant challenges.

11:45 Presentation to be Announced

12:15 pm Sponsored Presentation

(Opportunity Available)

12:30 Luncheon Presentation

(Sponsorship Opportunity Available)

1:15 End of Conference

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Cell Therapy Bioproduction

Overcoming the Development, Processing and Scale-Up/Out Dilemma

STREAM 4
Development of Next-Generation Biologics

Suggested Short Course*

Biophysical Characterization in Developing Biopharmaceuticals: The Path to Developability, Stability and Comparability

Thursday, August 21, 6:30- 9:00 pm

**Separate registration required; see page 3 for details*

THURSDAY, AUGUST 21

1:55 pm Chairperson's Remarks

David J. Williams, Ph.D., Professor, Healthcare Engineering, Centre for Biologics Engineering, Loughborough University

» FEATURED PRESENTATION

2:00 The Dawn of a New Day for Tissue Engineering: Applications Enabled by Cell Manufacturing Innovations

Jon A. Rowley, Ph.D., Chief Executive and Technical Officer, RoosterBio

The cell therapy Product Innovations of the early 2000s has led to the expected Manufacturing Process Innovations over the last few years. The latter has led to increased lot sizes and a focus on decreasing COGS of the cellular products that are moving through late stage clinical trials. As the cost of therapeutic cells decreases and availability of cells increases, new fields that require abundant and affordable high quality cells, such as tissue engineering and bioprinting, will begin to accelerate.

KEY CONCEPTS IN PRECISION MANUFACTURING AND COST-OF-GOODS

2:45 Precision Manufacturing of Living Materials – Working It Out for Cell Therapies

David J. Williams, Ph.D., Professor, Healthcare Engineering, Centre for Biologics Engineering, Loughborough University

The presentation will introduce key concepts of precision manufacturing in particular that of process capability. It will then discuss the key manufacturing scenarios for cell therapies with respect to the fundamentals of Good Manufacturing Practice and variation and it's control with a focus on biological variation. It will close by identifying the particular issues on which the cell therapy community should work together pre-competitively in order to facilitate the development and manufacturing of cell therapies.

3:15 Understanding Cell Therapy Cost of Goods – Linking Detailed Analysis to Industry Challenges

Mark McCall, Ph.D., Enterprise Fellow, Loughborough University

The presentation will introduce how detailed analysis of manufacturing systems and business models can produce reliable estimates of Cost of Goods for cell therapies. It will then discuss several scenarios with specific case studies performed using an activity based cost model. . It will finish by identifying the particular issues that this model has identified as current production bottlenecks for the cell therapy community and propose mitigation strategies to address these.

3:45 Sponsored Presentation

(Opportunity Available)

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

4:45 Breakout Discussions

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. At the end of the session, each moderator will summarize the topics being discussed, the findings and conclusions (if any), and share with the audience.

5:45 End of Day

5:45 – 6:30 Dinner Short Course Registration

6:30 – 9:00 Dinner Short Course*: Biophysical Characterization in Developing Biopharmaceuticals: The Path to Developability, Stability and Comparability

**Separate registration required; see page 3 for details*

FRIDAY, AUGUST 22

8:00 am Registration and Morning Coffee

ANALYTICAL CHARACTERIZATION: POTENCY ASSAYS, RELEASE TESTING AND CONTROL STRATEGIES

8:25 Chairperson's Remarks

Mark Angelino, Ph.D., Vice President, Pharmaceutical Sciences, bluebird Bio

8:30 Translating a Research Methodology into a Mechanism of Action Based Validated Potency Assay

Sagi Nahum, Ph.D., QC Manager, Pluristem Therapeutics, Inc.

Validated potency assays aims to measure or predict the expected therapeutic mechanism of action (MOA). Clinical data may be used to establish a correlation between potency assays allowing lot release and stability. Most of the potency assays emerge from research and academy transforming to potency assays after a long journey of validation. The talk will describe the path and challenges of bioassay development from research to QC based on Pluristem Therapeutics experience.

9:00 Autologous Lots of Cell Therapy Products: Potency Defined by Commonality

Don Healey, Ph.D., CSO, Opexa Therapeutics

Autologous lots of cell therapy products invariably display differences in either phenotype and/or genotype, as may be a requirement to meet their intended mechanism of action on a per patient basis. Nevertheless, potency can be defined based on biological features that must be held 'in common' between products that achieve the intended clinical benefit. The development of potency assays should be multi-factorial in the first instance, and should be initiated early in the process development timeline.

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Inaugural

Cell Therapy Bioproduction

Overcoming the Development, Processing and Scale-Up/Out Dilemma

STREAM 4
Development of Next-Generation Biologics

9:30 Critical Quality Attributes (CQA) Identification for a Cell-Based Gene Therapy Product, Approaches to Selection and Validation of Release Test Methods

Bernadette Keane, BSc., Vice President, Quality, Bluebird bio

In the emerging fields of cellular and gene therapy, control strategies are not yet well defined and pose their own set of challenges due to inherent variability of living systems. Using examples from autologous cell based gene therapy products, the presenter will discuss approaches to validation of test methods employed in the release of cell based gene therapy products.

10:00 Mid-Morning Snack in the Exhibit Hall with Poster Viewing

10:45 Rapid Microbiological Methods to Enhance Safety Profile of Cell-Based Therapeutics

Gary C. du Moulin, Ph.D., MPH, RAC, Senior Director, Quality Aseptic Controls, Genzyme (a Sanofi Company)

Cell-based therapeutics has accelerated Rapid Microbiological Methods implementation. In 2004, the United States Food and Drug Administration (FDA) approved an RMM for lot release of Genzyme's cell therapy product, Carticel®. Globalization of pharmaceutical quality systems, which emphasizes risk assessment and continual improvement of manufacturing processes has further accelerated acceptance of these technologies. RMM have the ability to identify microbiological risks, monitor critical control points in real time thus enhancing the safety profile of cell therapy products.

SCALING-UP/OUT AND PROCESS OPTIMIZATION

11:15 Scale-Up and Optimization of an Allogeneic Cell Therapy Process

Hari Kamaraju, Ph.D., Senior Associate Scientist, Pharmaceutical Development & Manufacturing Sciences, Janssen Research & Development

11:45 Optimization of T Cell Production Process for Adoptive T Cell Therapy

Pranay Khare, Ph.D., Director, Research, Cancer Immunotherapy and Gene Therapy cGMP Facility, Roger Williams Medical Center

Adaptive T cell therapy has showed promising results in several clinical trials for leukemia, but limited success has been achieved in solid tumors. Almost all clinical studies have used interleukin-2 as primary cytokine for the T cell production and expansion process. This talk will focus on the optimization protocol for T cell production process using other common gamma-chain family cytokines of T cell, and explore the therapeutic response of T cells for solid tumors using adoptive T cell therapy approach.

12:15 pm Sponsored Presentations

(Opportunities Available)

12:45 Luncheon Presentation: Single-Use Expansion and Harvest of Adult Stem Cells Supports Large-Scale Manufacturing

Sponsored by

Julie R. Murrell, Ph.D., Program Manager, Collaborations; R&D Manager, EMD Millipore Corporation

As more stem cell therapeutics progress through clinical testing, current *in vitro* culture methods are cumbersome to scale. Here we describe a case study for full expansion, harvest and characterization system for hMSCs. In this work, we verified that cells expanded in the single-use stirred tank bioreactor and subsequently harvested were identical in phenotypic and genotypic profile in comparison to flat culture and maintained the desired cell characteristics of hMSCs, thereby confirming the consistency, quality and reproducibility of large-scale *in vitro* systems for stem cell expansion.

STRATEGIES FOR CLINICAL TO COMMERCIAL MANUFACTURING

1:55 Chairperson's Remarks

Ravinder Bhatia, Associate Director, Pharmaceutical Development and Manufacturing Sciences, Johnson & Johnson

2:00 Strategy to Commercialize Autologous Cell Therapies

Knut Niss, Ph.D., Senior Technical Project Leader, Novartis Pharmaceuticals Corp.

2:30 From Development Through Approval of An Autologous Cell Therapy

Stephen J. Duguay, Ph.D., Associate Director, Process Development, Aastrom Biosciences

3:00 Refreshment Break

3:15 The Road Not Taken… Moving Cell Therapy from Benchtop to an Industry

Ohad Karnieli, Ph.D., MBA, Vice President, Development and Manufacturing, Pluristem Therapeutics, Israel

The need for large quantities of cells with high quality becomes crucial as product candidates advance into clinical trials. Technologies are evolving to allow production of large quantities. Nevertheless, high quantities of cells opens new questions and challenges of cell quality, identity, reproducibility and cost. The talk will describe the development of the GMP manufacturing technology for PLX (PLacental eXpanded) cell product candidates and some of the bottlenecks encountered in Pluristem's pilot and manufacturing facilities.

» FEATURED PRESENTATION

3:45 Towards Bioengineered Control of Cell Fate Post Transplantation

Jeffrey M. Karp, Ph.D., Associate Professor of Medicine, Brigham and Women's Hospital, Harvard Medical School

Control of cell fate and its extracellular environment following transplantation is critical for maximizing efficacy of cell based therapy. This talk will explore methods to enhance the engraftment and tracking of systemically infused stem cells through engineering the cell surface and through functionalizing cells with contrast agents and depots containing phenotype altering agents.

4:45 End of Conference

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Discounted Room Rate: $229 s/d
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