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NINTH ANNUAL

# THE BIOPROCESSING SUMMIT

## Practical Solutions for Today's Bioprocess Challenges

**AUGUST 21-25, 2017 | BOSTON, MA**

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*Give yourself a Bioprocess Holiday this summer!*

*Stimulate and enrich yourself at the 9th Annual The Bioprocessing Summit — the leading bioprocess event!*

## ABOUT THE SUMMIT

The Bioprocessing Summit brings together over 1,200 bioprocess professionals from around the world to share practical solutions for today's bioprocess challenges. The 9th annual event has grown to include 18 distinct meetings with weeklong coverage of upstream and downstream processing, analytical development and quality, formulation and stability, cell and gene therapy production, and manufacturing. Along with the impressive array of conferences, the Summit also includes Short Courses and Training Seminars that delve deeply into important bioprocess topics.

## EVENT AT A GLANCE

*Click on track title to view agenda*

| Monday - Tuesday (August 21-22) | Wednesday - Thursday AM (August 23-24) | Thursday PM - Friday (August 24-25) |
|---|---|---|
| Optimizing Cell Culture Technology | Bioproduction: Scale, Bioreactors & Disposables | Optimizing Cell Line Development |
| Continuous Processing in Biopharm Manufacturing | Advances in Purification Technologies | Virus & Pathogen Clearance & Safety in Biologics |
| Host Cell Proteins: Detection, Analysis & Removal | Early Analytical Development for Biotherapeutics | Process Characterization & Control |
| Rapid Methods to Assess Quality & Stability of Biologics<br>Overcoming Formulation Challenges | High-Concentration Protein Formulations | Introduction to Biologics Formulation & Delivery |
| Cell Therapy CMC, Quality & Analytics | Cell Therapy Manufacturing, Operations & Logistics | |
| | Gene Therapy CMC & Analytics | Gene Therapy Bioproduction |
| Continuous Processing in Biopharm Manufacturing | Manufacturing Efficiencies & Process Improvement | CMC Strategies for Antibody-Drug Conjugates |
| Introduction to Bioprocessing<br>Introduction to Extractables & Leachables & Packaging<br>Regulatory Requirements across the Product Development Lifecycle<br>Basic Technologies in a Protein Production Lab | Introduction to Cell Culture<br>Pharmaceutical Biotechnology Discovery: From Antibody Engineering to Gene Therapy | Introduction to Analytical Method Development & Validation for Therapeutic Proteins<br>Introduction to Downstream Processing<br>Introduction to Biologics Formulation & Delivery<br>Designing Flexible Facilities for Bioprocess Development & Manufacturing |
| **SHORT COURSES***<br>Monday, August 21 - 9:00–11:30 am | **DINNER SHORT COURSES***<br>Tuesday, August 22 - 6:00–8:30 pm | **DINNER SHORT COURSES***<br>Thursday, August 24 - 6:00–9:00 pm |

**Separate registration required*

# PLENARY KEYNOTE SESSION

## Wednesday, August 23 (4:45 - 6:00pm)

*Chairperson:*
*John Sterling, M.A., Editor-in-Chief, Genetic Engineering & Biotechnology News*

**4:50 Protein Aggregation and Oxidation during Processing**

*Jean-René Authelin, Ph.D., Global Head, Pharmaceutical Engineering, Sanofi*

Proteins are known to be sensitive to many stresses, including oxidation and shear stress, leading to potentially immunogenic aggregates. In this talk, we will present theoretical aspects together with real-life industrial examples illustrating the possible traps we may find in the fill & finish processing. We will, as well, propose the experiments that need to be performed in order to understand and predict the risk and the practical industrial solutions to implement solutions accordingly.

**5:25 Practical, Proven and Innovative Solutions for Today's Manufacturing Challenges**

*Thomas Seewoester, Ph.D., Executive Director and Plant Manager, Amgen Rhode Island*

Amgen's Rhode Island facility is among the largest drug substance production facilities in the world and is a cornerstone in Amgen's global production network. We will share some practical, proven and innovative solutions to achieve reliable, efficient and agile multi-product and multi-process manufacturing operations aimed at providing uninterrupted global supply.

**6:00 Close of Plenary Session**

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View Current Exhibitor List and Floor Plan

# Training SEMINARS

By Cambridge Healthtech Institute

## MONDAY, AUGUST 21 – TUESDAY, AUGUST 22, 2017

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

### TS1A: Introduction to Bioprocessing

This training offers a comprehensive survey of the steps needed to produce today's complex biopharmaceuticals, from early development through commercial. The seminar begins by introducing biologic drugs and the aspects of protein science that drive the progression of analytical and process steps that follows. We then step through the stages of bioprocessing, from cell line development to scaling up for commercial production. The seminar explores emerging process technologies, facility design considerations and the regulatory and quality standards that govern development. The roles of analytical methods at all stages as well as formulation and stability assessments in developing and gaining approval are also examined.

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

*Frank J. Riske, Ph.D., Senior Consultant, BioProcess Technology Consultants, Inc.*

### TS2A: Introduction to Extractables and Leachables and Packaging

This 1.5-day training seminar will provide a background on regulatory expectations for materials and components in contact with biologics and the unique applications to biologic delivery systems. Sources of leachables will be realized by understanding components of delivery systems as related to the physical and chemical requirements for various delivery systems. Attendees will be shown how to design studies to understand material chemistry through extractable studies and correlation to potential leachables. These learnings will put into perspective the current regulations and provide a means to develop best practices to manage extractables and leachable issues by applying science and risk based approaches for assessing extractables and acquiring appropriate information to support regulatory submissions.

*Instructors:*
*Diane Paskiet, MS, Senior Director, Global Scientific Affairs, West Pharmaceuticals*

*Kimberly Ehman, Ph.D., Director, Technical and Regulatory, WuXi AppTec*

### TS3A: Regulatory Requirements across the Product Development Lifecycle

This course provides a comprehensive review of the Chemistry, Manufacturing and Controls (CMC) section of regulatory filings, with a focus on phase appropriate requirements. The level of detail that must be included in the filing will be discussed as well as systems and controls that must be in place in the manufacturing setting. Topics such as process development, analytical development, Good Manufacturing Practices (GMP) and Good Laboratory Practices (GLP) will be discussed in the context of the stage of drug development. Regulatory strategies for navigating the path to approval will also be discussed. This course provides a broad understanding of regulatory requirements across the product development lifecycle.

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

### TS4A: Basic Technologies in a Protein Production Lab

This seminar is designed to introduce basic technologies, strategies and considerations in recombinant protein production in *E. coli*, insect and mammalian cells for multiple research and development applications. The seminar supplies a basic toolbox for management of multiple and diverse projects.

Who should attend: The seminar is designed for researchers, lab managers, graduate students, postdocs, technicians and engineers wishing to expand their knowledge and implement basic and advanced technologies in recombinant protein production in their work.

*Instructors:*
*Tsafi Danieli, Ph.D., Director, BioGivExcubator & Head, Protein Expression Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem*

*Mario Lebendiker, Ph.D., Head, Protein Purification Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem*

## WEDNESDAY, AUGUST 23 – THURSDAY, AUGUST 24, 2017

**DAY 1** - 8:00 AM – 6:00 PM
**DAY 2** - 8:00 AM – 12:15 PM

### TS5B: Pharmaceutical Biotechnology Discovery – From Antibody Engineering to Gene Therapy

This course will introduce the field of Pharmaceutical Biotechnology in a dynamic manner, starting with historical aspects, from the natural products era to the era of recombinant proteins, genes and cells. New therapeutic modalities such as gene therapy, recombinant cell therapy, bispecific antibodies, silencing RNA technologies, and gene editing are being used to treat diseases that were never able to be addressed properly using classical small molecule approaches. The course will delve into current strategies and concepts for treating and even curing diseases that were thought to be untreatable. It will finish by looking toward the future and comparing the landscape of 2025 with that of 2005, demonstrating how technologies have advanced the state of medical sciences like never before.

*Instructor:*
*William Strohl, Founder and Owner of BiSTro Biotech Consulting, LLC*

### TS6B: Introduction to Cell Culture

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.

*Instructor:*
*Kamal Rashid, Ph.D., Director & Research Professor, Biomanufacturing Education & Training Center, and Biology/Biotechnology Department, Worcester Polytechnic Institute*

# Training SEMINARS

By Cambridge Healthtech Institute

## THURSDAY, AUGUST 24 – FRIDAY, AUGUST 25, 2017

**DAY 1** - 1:30 PM – 5:30 PM
**DAY 2** - 8:30 AM – 3:30 PM

### TS8C: Intro to Downstream Processing

This activity-packed course focuses on the science, technologies and strategies needed to understand and implement an effective downstream process for biological development and production. The course begins with an in-depth look at DSP design and development - from recovery to purification to formulation - before moving onto pertinent issues surrounding HTPD, single-use systems, continuous processing, PAT, viral clearance, platform development, process validation and bioprocess simulation. The course will be based on real-world examples from downstream development projects for both traditional and emerging modalities. Students will learn through on-site exercises and use of computational tools.

*Instructor:*
*Jean-François Hamel, Ph.D., Academic Researcher and Instructor, Chemical Engineering Department, Massachusetts Institute of Technology; Biotech Programs, Northeastern University*

### TS9C: Introduction to Analytical Method Development and Validation for Therapeutic Proteins

This course is a panoramic review of analytical method development and validation for therapeutic proteins, including antibodies and enzymes. It starts with basic knowledge of work on therapeutic proteins: manufacturing of protein drugs, regulatory affair knowledge and protein chemistry. It then discusses fundamentals and practical aspects of commonly used analytical methods for proteins, including methods for structure elucidation, glycan characterization, biophysical characterization, potency measurement, purity and impurity analysis. The course concludes with the strategy and common practice in method validation and method transfer, including regulatory compliance at different stages of product development, application of DOE and QbD. The course emphasizes practical applications, real-world examples and useful tips.

*Instructor:*
*Jichao (Jay) Kang, Ph.D., RAC, Director, Analytical and Formulation Development, Patheon Biologics*

### TS10C: Introduction to Biologics Formulation and Delivery

The formulation training seminar focuses on strategies to plan and execute preformulation and formulation development studies for biologics that require co-optimization of multiple physical, chemical, and conformational stability attributes under accelerated timelines to ensure rapid delivery of a stabile product to the clinic. The seminar begins with an overview of biophysical and biochemical properties of proteins and protein structure, setting the stage for the concepts at the core of protein formulation, then explores the theory and application of the relevant analytical and biophysical techniques that support preformulation and formulation development studies. The course then concludes with examination of real-world case studies.

*Instructor:*
*Donald E. Kerkow, Ph.D., Associate Director, Biopharmaceutical Development, KBI Biopharma, Inc.*

### TS11C: Designing Flexible Facilities for Bioprocess Development and Manufacturing

Biomanufacturing organizations today are looking for best practice approaches to create flexible manufacturing assets to support overall business needs. With expanding product pipelines and the introduction of new technology platforms, creating an asset that will not only have a long lifecycle expectancy but one that will also be flexible to meet development and commercial launch needs is a paramount business goal.

This two-day course will introduce attendees to the key facility design considerations that are needed to ensure the creation of a design concept and approach that will yield highly flexible, optimized, and highly utilized manufacturing assets. Key concepts will include development and understanding of a manufacturing enterprise model, the product-process-facility paradigm, "design-to-operate" methodology, appropriateness of GMP design compliance, and the identification and mitigation of risks around a sound QRM approach.

The course will implement traditional lecture components, class exercises, and the use of case studies as learning tools.

*Instructor:*
*Jeffery Odum, MSc, CPIP, Global Technology Partner, NNE Pharmaplan; Managing Partner, Strategic Manufacturing Concept Group*

Each CHI Training Seminar offers 1.5 days of instruction with start and stop times for each day shown above and on the Event-at-a-Glance published in the onsite Program & Event Guide. Training Seminars will include morning and afternoon refreshment breaks, as applicable, and lunch will be provided to all registered attendees on the full day of the class.

Each person registered specifically for the training seminar will be provided with a hard copy handbook for the seminar in which they are registered. A limited number of additional handbooks will be available for other delegates who wish to attend the seminar, but after these have been distributed, no additional books will be available.

Though CHI encourages track hopping between conference programs, we ask that Training Seminars not be disturbed once they have begun. In the interest of maintaining the highest quality learning environment for Training Seminar attendees, and because Seminars are conducted differently than conference programming, we ask that attendees commit to attending the entire program, and not engage in track hopping, as to not disturb the hands-on style instruction being offered to the other participants.

CLICK TO VIEW

Full Training Seminar Agendas and Instructor Biographies

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# SHORT COURSES*

## MONDAY, AUGUST 21, 2017

**9:00 – 11:30 am**

**SC1: Optimizing Cell Culture Media – Achieving Super Soup**
*Kamal Rashid, Ph.D., Director & Research Professor, Biomanufacturing Education & Training Center, and Biology/Biotechnology Department, Worcester Polytechnic Institute*
*Jochen B. Sieck, Ph.D., Head, Perfusion Systems Laboratory, Perfusion Systems and Cell Culture Media R&D, Merck Life Science*
*Sven Loebrich, Ph.D., Development Scientist III, Upstream Process Engineering, Immunogen, Inc.*

**SC2: Comparability Strategies for Cell and Gene Therapies**
*Christopher Bravery, Ph.D., Consulting Regulatory Scientist, Consulting on Advanced Biologicals Ltd.*

**SC3: Advanced Process Control, Intensified DoE and Hybrid Modeling for Process Optimization and Characterization**
*Gerald Striedner, Ph.D., Associate Professor, Biotechnology (BOKU), Principal Investigator, Austrian Center of Industrial Biotechnology (ACIB)*
*Martin Mayer, Head, Business Development, evon GmbH*

**SC4: Accelerated Stability Testing of Biologics**
*Jan Jezek, Ph.D., CSO, Development, Arecor Ltd.*

## Dinner Short Courses

## TUESDAY, AUGUST 22, 2017

**6:00 – 8:30 pm**

**SC5: Potency Assay Development for Cell and Gene Therapy Products**
*Christopher Bravery, Ph.D., Consulting Regulatory Scientist, Consulting on Advanced Biologicals Ltd.*

**SC6: Integrated Continuous Biomanufacturing - An Implementation Approach: Planning, Technology, Regulatory, and Manufacturing Advantages to Present Robust Optimized Batch Manufacturing**
*Robert Dream, Managing Director, HDR Company, LLC*

**SC7: Analytical Strategies for Comparability in Bioprocess Development**
*Christine P. Chan, Ph.D., Principal Scientist/Technical Lead, Global Manufacturing Science & Technology, Specialty Care Operations, Sanofi*

**SC8: Protein Aggregation: Mechanism, Characterization and Consequences**
*Tom Laue, Ph.D., Professor Emeritus, Biochemistry, University of New Hampshire*

## THURSDAY, AUGUST 24, 2017

**6:00 – 9:00 pm**

**SC9: Transient Protein Production in Mammalian Cells**
*Richard Altman, MS, Scientist V, Protein Technologies, Amgen*
*Henry C. Chiou, Ph.D., Associate Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific*
*Dominic Esposito, Ph.D., Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research*
*Panelist: Bojiao Yin, Ph.D., Researcher, Protein Technologies, Amgen*

** Separate registration required*

# Upstream Processing

The weeklong Upstream Processing stream covers the foundations of protein expression, including Cell Line Development and Cell Culture. The stream also delves into Bioproduction issues such as developing representative small-scale models, scaling up production, optimizing bioreactors, and integrating disposables into processes. Throughout the week, case studies and helpful protocols are shared to help researchers with their jobs at the bench, all with an eye to increasing titers and productivity in bioprocessing.

## 2017 UPSTREAM PROCESSING TRACKS

**AUGUST 21-22**
AGENDA Optimizing Cell Culture Technology

**AUGUST 23-24**
AGENDA Bioproduction: Scale, Bioreactors & Disposables

**AUGUST 24-25**
AGENDA Optimizing Cell Line Development

# Optimizing Cell Culture Technology

Enhancing Knowledge for Growing Cells



## MONDAY, AUGUST 21

**8:00 am Short Course Registration Open**

**9:00 – 11:30 Recommended Morning Short Courses***

**SC1: Optimizing Cell Culture Media**

** Separate registration required, see page 6 for details.*

**11:30 Main Conference Registration Open**

## IMPROVING CELL CULTURE PROCESSES & PRODUCTIVITY

**1:00 pm Chairperson's Opening Remarks**

*Alan Dickson, Ph.D., Director, Centre of Excellence in Biopharmaceuticals (COEBP), and Professor, Biotechnology, The University of Manchester*

**1:10 OPENING KEYNOTE PRESENTATION:**

**Innovations in Process Science within an End-to-End Integrated Development Organization, Delivers on Speed, Cost and Quality Objectives for Biogen's Biotherapeutic Pipeline**

*Rashmi Korke-Kshirsagar, Ph.D., Director, Cell Line and Cell Culture Development for Proteins, Biogen*

Biogen has developed platform approaches for our various unit operations. Investment in process sciences, innovation and technology development were enabling factors and will be discussed. This has allowed us to routinely deliver high-productivity processes for early clinical programs. During late-stage process development and characterization of the processes and the quality attributes, we have realized the value of end-to-end integration of DS and DP development organization. Deep bioprocess knowledge and understanding coupled with integrated analytical characterization and formulation development has delivered the optimal solution of high volumetric productivity, low-cost manufacturing, and desired product quality. Optimization of this knowledge has translated into the end- to-end early and late-stage approach for our future pipeline.

**1:45 Cell-Derived Extracellular Matrix: Isolation, Analysis and Functional Studies**

*Josephine C. Adams, Ph.D., Professor, Cell Biology, Biochemistry, University of Bristol*

Metazoan extracellular matrix (ECM) consists of fibres and networks of collagens, glycoproteins and proteoglycans. The ECM micro-environment has important roles in cell survival, differentiation, motility and mechanical force-balance in tissues. Isolation of ECM is complicated by its insoluble, cross-linked nature and the need to separate ECM from cellular proteins. I will discuss my laboratory's approaches with a scaleable method to isolate ECM from adherent, cultured cells for downstream experimentation.

**2:15 Use of Multivariate Data Analysis to Improve Cell Culture Performance in a Commercial Process**

*Betty Agudelo-Rewey, M.S., Principal Engineer, Drug Substance Process Development, Amgen, Inc.*

Process variability can lead to poor process performance and can impact product quality attributes. Cell culture manufacturing processes are multivariate by nature which can make it more difficult to determine the sources of input variation and therefore make it more difficult to diagnose and troubleshoot issues. The application of appropriate multivariate data analyses can significantly aid in signal identification, diagnosis, understanding of process shifts, as well as in the identification of improvement opportunities. A case study will be presented to demonstrate the value of this approach to control variation for a critical quality attribute while maintaining process performance.

**2:45 Refreshment Break**

## IMPROVING CELL CULTURE PROCESSES & PRODUCTIVITY

**3:15 From CHO to hMSCs, Perceptions and Reality of "Shear Sensitivities"**

*Jeffrey Chalmers, Ph.D., Professor, Chemical and Biomolecular Engineering, The Ohio State University*

Suspension animal cell culture is now routinely scaled up to bioreactors on the order of 10,000 liters, and greater, to meet commercial demand. However, the concern of the "shear sensitivity" of animal cells still remains, not only within the bioreactor, but also in the downstream processing. The perception of "shear sensitivity" has historically put an arbitrary upper limit on agitation and aeration in bioreactor operation. 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.

**3:45 ChemStress Fingerprinting: A Simple, Novel Process Control Strategy for CHO Cell Factories**

*Sponsored by* valitacell

*Jerry Clifford, Ph.D., MBA, COO, Valitacell*

Valitacell is developing technologies that have been specifically designed to provide a desired level of process control while at the same time enabling optimal leverage of the cell factory for each individual product. Here we discuss new methodologies to measure and predict clone-specific functional stability using rapid, multiparallel ChemStress fingerprinting.

**4:00 Understanding and Modulating the Quality Attributes of a Novel Class of Therapeutic Proteins through Upstream Process Development**

*Ravindra Pangule, Ph.D., Associate Principal Scientist, Process Development & Engineering, Merck Research Laboratories*

Next-generation biotherapeutic proteins, engineered with unique and novel biology, have attracted more attention in recent years. However, understanding and controlling the quality attributes for those proteins are still in early stages. I will share our experience with two molecules from a novel class of therapeutic proteins as case studies. I will present the strategies designed and implemented to address product quality liabilities associated with these molecules. Specifically, media supplementation and process optimization approaches were taken to control post-translational modifications and product-related impurity levels.

**4:30 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.

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

**7:00 Close of Day**

## TUESDAY, AUGUST 22

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

## ENHANCING THE CULTIVATION ENVIRONMENT

**7:55 Chairperson's Remarks**

*Jeffrey Chalmers, Ph.D., Professor, Chemical and Biomolecular Engineering, The Ohio State University*

**8:00 Is It Time to Reinvent Basic Cell Culture Medium?**

*Svetlana V. Komarova, Ph.D., Associate Professor, Dentistry, McGill University*

The quality of the cell culture media is critically important for the success of *in vitro* experiments. Four synthetic media formulations developed more than 50 years ago – DMEM, RPMI 1640, MEM, and Medium 199 (M199) – are used in ~90% of published *in vitro* studies. However, the levels of electrolytes and carbohydrates in these media formulations largely deviate from physiological values. The potential consequences of such deviations will be discussed.

**8:30 Systems Biology Approach in the Development of Chemically-Defined Media for Production of Protein Therapeutics in CHO Cells**

*Wai Lam W. Ling, Ph.D., Senior Principal Scientist and Group Director, Process Development & Engineering, Biologics & Vaccines BioProcess Development, Merck Research Labs*

**9:00 Assessing Mycoplasma Contamination of Cell Cultures by qPCR using a Set of Universal Primer Pairs Targeting a 1.5 kb Fragment of 16S rRNA Genes**

*Denis Gerlier, M.D., Ph.D., Emeritus Director of Research, CNRS, International Center for Infectiology Research (CIRI), SFR Bioscience, University of Lyon*

Mycoplasma are a formidable threat both in fundamental research by perverting a whole range of cell properties and functions, and in the pharmacological use of cells and cell-derived products. I shall report a universal, sensitive, and quantitative assay based on the amplification of a 1.5 kb fragment covering the 16S rDNA of the Mollicute class, and its usefulness to check mycoplasma contaminations in BSL2, BSL3 and BSL4 viral stocks.

**9:30 Improve Efficiency and Eliminate Human Error with Automated Sampling and Feed Control**

*Sponsored by* Flownamics

*Frederick Schneider Jr., Director of Sales, Flownamics*

What if you could reduce or completely eliminate the time spent sampling manually each day and or on weekends? In this technical seminar, you will learn how the Seg-Flow automated sampling platform will improve your process conditions and performance, decrease sample volume requirements and save you both time and money.

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

## MONITORING QUALITY

**10:30 Quality by ~~Design~~ Control or Why We Could use a Different Understanding of the Design Space**

*Moritz von Stosch, Ph.D., Senior Manager, Fermentation, GlaxoSmithKline Pharma GmbH*

Real-time control of the critical product quality attributes via appropriate manipulation of the process parameters requires:

1) Understanding how the process parameters impact on the quality attributes

2) The quality attributes to be measurable in some form on-line.

Astonishingly (or not), the Quality by Design (QbD) roadmap, looks much like a guide to realize real-time product quality control, only that process dynamics seem to be overlooked. In this contribution, the implications of considering the process dynamics in the QbD roadmap are discussed and a strategy for exploiting the dynamics in an intensified Design of Experiment method is demonstrated, which can significantly reduce the number of experiments required to achieve process understanding.

**11:00 SPR Biosensing of Monoclonal Antibody during Cell Culture**

*Gregory De Crescenzo, Ph.D., Professor, Chemical Engineering, Polytechnique de Montréal*

A surface plasmon resonance-based assay has been developed to quantify monoclonal antibody within the supernatant of a mammalian cell and confirm Mab binding to its antigen in a single biosensing experiment. Our results were in excellent agreement with quantification performed by Protein-A HPLC. While the approach is of interest for off-line analysis, its application to at-line characterization will be discussed.

**11:30 Softsensors: New Approach for Process Monitoring Cell Growth in Small-Scale Fermentation Systems**

*Wolfgang Paul, Ph.D., Group Leader, Cell Culture Research, Roche Innovation Center Munich, Roche Diagnostics GmbH*

The new approach is a soft sensor, which takes online signals of the bioreactor, which are correlated to cell growth to estimate the cell growth. The soft sensor based on multiple linear regression and on artificial neural network to estimate the cell growth as online signal during cultivation time. The soft sensor was successful implemented in the multiple small scale bioreactor system and estimated values with high confidence and low root mean squared error below 15%.

**12:00 pm Using Metabolomics to Understand Genetically Determined and Environmental Cell Culture Needs**

*Sponsored by* METABOLON

*Kendra Hightower, Ph.D., Study Director, Metabolon*

**12:30 Luncheon Presentation: "Difficult-to-Express" Proteins: Solutions for Clinical Manufacturing**

*Sponsored by* C3 CELL CULTURE COMPANY

*Scott Waniger, Vice President, Bioprocessing, Cell Culture Company*

Advances in protein engineering have made complex biologic therapeutics more prominent. These molecules are sometimes labeled as "difficult-to-express" proteins due to low protein titers and/or sensitivity to environmental conditions, making clinical manufacturing slow and expensive. Acusyst

perfusion systems provide an alternative to traditional fed-batch systems for clinical manufacturing, enabling efficient production of difficult-to-express proteins. This talk presents case studies demonstrating the benefits of Acusyst systems including enhanced yields, reduced costs and improved scalability.

**1:15 Dessert Refreshment Break in the Exhibit Hall with Poster Viewing**

## CULTIVATING CHO CELLS FOR MANUFACTURING

**1:55 Chairperson's Remarks**
*Shahram Misaghi, Ph.D., Senior Scientist, Early Stage Cell Culture, Genentech -- A Member of the Roche Group*

**2:00 FEATURED PRESENTATION:**
**Genome Editing of CHO Cells: Molecular Tinkering or Revolutionary Change?**
*Alan Dickson, Ph.D., Director, Centre of Excellence in Biopharmaceuticals (COEBP), and Professor, Biotechnology, The University of Manchester*
What's new? Genome editing opens up the possibilities to revolutionise CHO cell platforms… or is it to discover that nature got there before us? In this case study, I will describe some of our recent work to engineer novel CHO cell phenotypes and focus on factors that maximisethe match between prediction and outcome.

**2:30 Population Dynamics in Cloned CHO Cell Lines**
*Jennifer Tzihsuan Lin, Ph.D., Senior Scientist, BioProcess R&D, Pfizer, Inc.*
The inherent nature of cloned CHO cell lines includes the presence of genetic and phenotypic drift that leads to heterogeneous populations. The genetic heterogeneity exhibited by these cells can be exploited to understand the population dynamics of cloned cell lines. Understanding the interplay between heterogeneity, cell culture conditions and population dynamics will allow for critical assessment of overarching cell line development methods and strategies in terms of population and monoclonality. Using sequence variants (SVs) as biomarkers to characterize and understand populations within cloned cell lines will be presented and monoclonality discussed.

**3:00 CRISPR Tools for CHO Cell Engineering**
*Helene Faustrup Kildegaard, Ph.D., Senior Researcher and Co-Principal Investigator, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark*
CHO cells are widely used in the industry as a host for the production of complex pharmaceutical proteins. Thus, accelerated genome engineering of CHO cell factories to improve product yield and quality is of great interest. In this talk, our recent efforts in accelerating genome engineering of CHO cell factories will be presented. Topics will include targeted integration and multiplexing of gene knockouts.

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

## BOOSTING CHO CELL CULTIVATION

**4:15 Advanced Process Monitoring and Hybrid Modeling: A Basis for QbD/PAT Implementation in Mammalian Cell Culture Bioprocesses?**
*Gerald Striedner, Ph.D., Associate Professor, Biotechnology, University of Natural Resources and Life Sciences (BOKU), and Principal Investigator, Austrian Center of Industrial Biotechnology (ACIB)*
- Advanced on- and offline monitoring strategies
- Implementation of hybrid modeling approaches in mAB production processes
- Transferability of hybrid models along scales from shaker to laboratory and pilot scale
- Towards Model predictive control (MPC) in bioprocesses

**4:45 BiP the Alarm; High Intracellular Seed Train BiP Levels Correlate with Poor Production Culture Performance, a Case Study of a DHFR-Deficient CHO Cell Line**
*Shahram Misaghi, Ph.D., Senior Scientist, Early Stage Cell Culture, Genentech -- A Member of the Roche Group*
Consistent cell culture performance is a prerequisite to ensure product quality consistency and achieve productivity goals to manufacture recombinant protein therapeutics, including monoclonal antibodies. To ensure a smooth transition from seed train through inoculum train to the production culture, parameters such as viability, viable cell count (VCC), packed cell volume (PCV), glucose consumption, and pH are closely monitored. Here we report a peculiar observation where high levels of intracellular BiP in seed train cultures are consistently predictive of poor cell culture performance in the subsequent inoculum and production cultures for a monoclonal antibody produced in CHO cells.

**5:15 Close of Conference**

**6:00 – 8:30 Recommended Dinner Short Course***

**SC7: Analytical Strategies for Comparability in Bioprocess Development**
*Christine P. Chan, Ph.D., Principal Scientist/ Technical Lead, Global Manufacturing Science & Technology, Specialty Care Operations, Sanofi*
** Separate registration required, see page 6 for details.*

# Bioproduction: Scale, Bioreactors & Disposables

Making It Work



## WEDNESDAY, AUGUST 23

**7:00 am Registration Open and Morning Coffee**

## IMPROVING CONDITIONS TO INCREASE PRODUCTIVITY

**8:05 Chairperson's Opening Remarks**

*Stefan Schmidt, Ph.D., M.B.A., Senior Vice President, Process Science and Production, Rentschler Biotechnology*

**8:15 OPENING KEYNOTE PRESENTATION:**

**Driving Continuous Improvements for Biologics Manufacturing**

*Kenneth D. Green, Ph.D., Head, Technical Services, Recombinant Protein Therapies, Shire Human Genetic Therapies*

This presentation will discuss opportunities for continuous improvement utilizing operational excellence and innovative approaches to deliver process robustness, manufacturing reliability, and productivity gains.

**9:00 FEATURED PRESENTATION:**

**Challenges with Biologics Process Development and Tech Transfer for Non-Antibody Non-Platform Molecules**

*Kumar Dhanasekharan, Ph.D., Senior Director and Head, Biologics Process and Analytical Development, Amicus Therapeutics*

This talk will address general challenges with process development for complex glycoproteins, including the use of cell culture perfusion and associated challenges, downstream challenges with HCP reduction, and also overall scalability and manufacturability of this important class of biologics. Dr. Dhanasekharan will offer insights with examples on tackling some of the challenges encountered.

**9:30 Cell Culture Scale Translation from a 24-Well Single-Use Miniature Bioreactor**

*Frank Baganz, Ph.D., Senior Lecturer, Biochemical Engineering, University College London (UCL)*

The need to bring new biopharmaceutical products to market more quickly and to reduce final manufacturing costs is driving early-stage, small-scale bioprocess development. This presentation will cover the engineering characterisation of a single-use 24-well parallel miniature bioreactor (MBR) in terms of power input, liquid phase mixing and oxygen mass transfer. Examples will be given for the application of this MBR to rationally scale cell culture processes.

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

*Sponsored by* ROCKLAND antibodies & assays

## IMPROVING CONDITIONS TO INCREASE PRODUCTIVITY

**10:45 Designing a 3-L Rigid SUB System: Characterization, Autosampling, Nutrient Control**

*T. Craig Seamans, Ph.D., Senior Principal Scientist, Bioprocess Technical Operations, MRL BioProcess Development, Merck & Co., Inc.*

The presence of resource-efficient systems for examining complex process options is key to effective upstream development. Here we report on enhanced design 3-L rigid single-use bioreactors (SUBs), coupled with completely automated sampling and feed control. The system can evaluate metabolic-based feed strategies for bench scale cell culture processes across multiple vessels. Implementation of the custom SUBs and automated sampling, has enabled enhanced process development capability, by introducing technology to both improve operational efficiency and provide a pragmatic new tool to study optimization and robustness.

**11:15 Improved Antibody Quality and Consistency in CHO Cells Using a Novel Media Supplement**

*Adam Elhofy, Ph.D., CSO, Bio-Ess Laboratories LLC*

There has been a push to improve consistency and quality of glycolytic patterns. Protein synthesis and post-translational modification occurs on the lipid membranes of the ER and Golgi. Addition of Cell-Ess improves the consistency and quality of glycosylation while also increasing titer. The use of Cell-Ess resulted in significantly less variation of the glycolytic pattern and increased higher order glycoforms. The novel method of adding lipids results in an improvement of protein quality and consistency.

**11:45 Cell Culture Scale-Up in BioBLU® c Rigid-Walled, Single-Use Bioreactors from Eppendorf**

*Sponsored by* eppendorf

*Stacey Willard, Ph.D., Senior Technical Applications Specialist – Bioprocess, Eppendorf*

Bioreactor scalability is critical for process development. We analyzed BioBLU Single-Use Vessels (maximum working volumes of 0.25L, 3.75L, 40L) and determined a scalable tip speed zone, kLa values, and using computational fluid dynamics simulations, power numbers. These data were used to scale-up a process for antibody production in CHO cells.

**12:15 pm Luncheon Presentation: Intensified Bioprocessing is Almost Here: An Update on Modular, End-to-End Continuous Automation**

*Sponsored by* Finesse

*Barbara Paldus, Ph.D., Vice President and General Manager, Finesse,a part of Thermo Fisher Scientific*

Continuous processing has been used successfully for many years in manufacturing industries such as food, chemicals, and steel. When applied to biomanufacturing and combined with single-use technology (SUT), continuous processing offers higher throughput and increased flexibility. SUT also enables the move from single-product processes to multi-product facilities. As transformative as SUT has been, the bigger shift will be combining single-use workstreams with continuous automation in a new modular architecture that reaches from inoculation through ultra-filtration.

**1:00 Session Break**

## SCALE-DOWN MODELS

**1:45 Chairperson's Remarks**
*Frank Baganz, Ph.D., Senior Lecturer, Biochemical Engineering, University College London (UCL)*

**1:50 Case Studies: Scale-Down Model Development and Optimization for Screening Raw Materials**
*Angela Au, Ph.D., Engineer II, Research & Development, Bristol-Myers Squibb Co.*
Understanding the relationship between key operating parameters and culture performance is dependent on having a robust scale-down model (SDM) which is an appropriate representation of the drug substance quality attributes and the proposed manufacturing scale. Raw material variability between suppliers and between lots can impact process performance. Case studies will demonstrate challenges with development and optimization of a SDM sensitive enough to screen raw materials for their impact at scale.

**2:20 Challenges in Developing a Representative Scale-Down Model**
*Shyamsundar Subramanian, Ph.D., Director, Biologics CMC, Teva Pharmaceuticals*
Due to the complexity and expense of manufacturing scale-process characterization, scale-down bioreactor models are essential. The biopharmaceutical industry has used different scaling and success criteria. This case study will highlight how challenges in developing a representative scale-down model were addressed for a CHO based antibody process.

**2:50 Scale-Down Model Development for a 5000-L Production Bioreactor Process Using 5-L Bioreactor Systems: A Case Study**
*Jeremy Discenza, M.Sc., Associate Scientist II, Bristol-Myers Squibb Co.*
A 5-L lab-scale bioreactor scale-down model (SDM) was developed to simulate monoclonal antibody production in a 5000-L bioreactor. The results of 5-L bioreactor runs demonstrated acceptable product quality but higher titer compared to the 5000-L production bioreactor. Process performance analysis culminated in a change in aeration strategy, resulting in a yield improvement at the commercial scale.

**3:20 Bioreactor Scale-Down Model Alterations to Better Predict Product Quality of Large Scale**
*Laurie Hazeltine, Ph.D., Research Scientist, Cell Culture – Late Phase, Eli Lilly and Company*
A scale-down model that accurately predicts cell growth, titer, and product quality is important for effective biopharmaceutical development. For one molecule in development at Lilly, difference in a critical quality attribute (CQA) was observed between small and large-scale bioreactors. While keeping scale independent parameters constant, other process parameters were investigated. Dissolved carbon dioxide was identified as one contributing factor to the CQA difference between scales. An improved scale-down model was developed to support the manufacturing control strategy.

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

**4:45 PLENARY KEYNOTE PRESENTATION**
*(See page 3 for details.)*

**6:00 Networking Reception in the Exhibit Hall with Poster Viewing**

**7:00 Close of Day**

## THURSDAY, AUGUST 24

**8:00 am Registration Open and Morning Coffee**

## INNOVATING PROCESSES

**8:25 Chairperson's Remarks**
*Jeremy Discenza, M.Sc., Associate Scientist II, Bristol-Myers Squibb Co.*

**8:30 Flexible and On-Demand Production of Therapeutic Biologics Using a Portable Device**
*Jicong Cao, Ph.D., Postdoctoral Associate, Biological Engineering, Massachusetts Institute of Technology (MIT)*
By combining genetic and hardware engineering, we developed a portable platform to produce multiple proteins on demand in an integrated microfluidic device. We created genetically engineered *Pichia pastoris* strains, which can produce one or more proteins of interest on programmable cues, and demonstrated the near-single-dose production of these biologics within 24 hours. The system allows people living in remote areas to get rapid access to therapeutic biologics at the point-of-care.

**9:00 Performance and Product Quality Implications of Bioreactor Perfusion via Single-Use Centrifugation vs. Tangential Flow Filtration**
*Rustin M. Shenkman, Ph.D., Senior Development Engineer, BDS Process Development, Shire*
A perfusion bioprocess for a therapeutic protein was developed for tangential flow filtration (TFF) and single-use centrifugation technologies. TFF has a wider industry base and familiar scaling paradigm whereas as single-use centrifugation has a limited industry base but, unlike microfiltration, does not suffer from product retention. Cell culture performance and drug substance (DS) quality attributes were similar scales and retention technologies. However, DS produced via TFF had decreased room-temperature stability.

**9:30 Sponsored by: The Windshire Group, LLC Continued Process Verification and Process Monitoring Using ProcessPad**
*James Blackwell, Ph.D., MBA, President, The Windshire Group, LLC*

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

## DISPOSABLES & SINGLE-USE SYSTEMS

**10:45 Achieving Seamless Scale-Up and Technology Transfer – A Case Study in Single-Use Bioreactors**
*Ying Wang, Ph.D., Senior Scientist I, Manufacturing Sciences, AbbVie Bioresearch Center*
A systematic scale-up strategy is critical in enabling a rapid and robust technical transfer. For a program involving a CHO cell culture process, a combination of mass-transfer (kLa) studies, computational simulation and scale-down model experiments were used within this newly developed work-flow. Utilizing this approach, scale-up was successfully accelerated

(<4 months) with titer improvement and comparable product quality. The main lessons learned from this case study will be presented.

**11:15 Scale-Up of a High Cell Density Perfusion Culture Using Only Single-Use Systems**

*Richard Rohe, M.Sc., Scientist, API Large Molecule, Johnson & Johnson*

A case study will be presented on scale-up of a perfusion process from 10L bench-top bioreactor to 1000L SUB system connected to an external single-use cell retention system for production of a virus based product. Cells were grown in the seed bioreactor, 250L SUB system, to high cell density using a perfusion process to inoculate and infect cells with a virus stock at high cell density in the 1000L production bioreactor. To scale up the process, the seed and production SUB systems configuration were changed to connect single-use cell retention system, to implement an aeration strategy to meet OTR and to strip CO2 from the culture and to provide sufficient power per unit volume.

**11:45 Disposables in Bioprocessing: Catalogue or Customization – Options and Limits of Flexibility**

*Stefan Schmidt, Ph.D., M.B.A., Senior Vice President, Process Science and Production, Rentschler Biotechnology*

On the one hand, the recent success of disposables in bioprocessing is directly related to being off the shelf catalogue products which are mass produced at competitive prices. On the other hand, single-use equipment offers huge benefits through the ability of being customized and on-purpose designed. Due to many years of intense use of disposable material, we will give advice on the customization, the related flexibility benefits and strategies to successfully navigate between catalogue and customized products.

**12:15 pm Enjoy Lunch on Your Own**

**1:15 Dessert Refreshment Break in the Exhibit Hall and Last Chance for Poster Viewing**

**1:55 Close of Conference**

# Optimizing Cell Line Development

Enhancing Expression



## THURSDAY, AUGUST 24

**11:30 am Registration Open**

**12:15 pm Enjoy Lunch on Your Own**

**1:15 Dessert Refreshment Break in the Exhibit Hall and Last Chance for Poster Viewing**

## CELL LINE DEVELOPMENT FOR THE BIOPHARMA INDUSTRY

**1:55 Chairperson's Remarks**

*Michael Butler, Ph.D., Distinguished Professor Emeritus, University of Manitoba, and CSO, Cell Technology, National Institute of Bioprocessing Research & Training (NIBRT)*

**2:00 KEYNOTE PRESENTATION:**

**Efficient Cell Line Development for Production and Regulatory Success**

*Pamela Hawley-Nelson, Ph.D., Associate Director, R&D; Head, Cell Biology in Process Cell Culture, MedImmune, Inc.*

**2:45 Implementation of New Technologies in Cell Line Generation**

*Jan Schouten, Ph.D., Principal Scientist, Synthon Biopharmaceuticals BV*

High-producing, clonal cell lines are at the basis of a biopharmaceutical production process. Strategies will be discussed to obtain cell lines with a high probability of monoclonality in a short time-frame. In addition, state-of-the-art Next Generation Sequencing tools will be discussed to detect and de-select sequence variants in an early stage.

**3:15 Transient Protein Production: Harmonizing the Process from Construct Generation through Protein Characterization**

*Richard Altman, MS, Scientist V, Protein Technologies, Amgen*

A robust, flexible transient protein production facility provides critical support to drug discovery efforts. We will review the ongoing evolution of our protein production endeavors focusing on two critical components. The first is the strategic assembly of mammalian expression "tools" that gives us a toolbox capable of expressing diverse and challenging candidate proteins. The second is the harmonization of the entire protein production process thereby reducing turnaround times and increasing throughput.

**3:45 Replacing Resistance Genes with Non-Coding RNA for Cell Line Selection**

Sponsored by HocusLocus

*Ted Eveleth, CEO, HocusLocus Inc*

We will present a new and novel approach to cell line selection being developed in conjunction with the Austrian Center of Industrial Biotechnology. This approach replaces the traditionally used resistance genes with an siRNA coupled to the gene of interest transcription and performs selection using transfected mRNA.

**4:00 Refreshment Break**

## DEVELOPING CHO CELL LINES

**4:15 Sequencing the CHO DXB11 Genome Reveals Regional Variations in Genomic Stability and Haploidy**

*Christian Schrøder Kaas, Ph.D., Postdoctoral Researcher, Expression Technologies, Novo Nordisk A/S*

The copy number from each gene in the genome was calculated from next-generation sequencing data revealed an unexpected degree of haploidy in Chinese Hamster Ovary (CHO) cells. The data can further be mined in order to reveal areas of the genome shown to be stable such as chromosome one and four, which can be hypothesized to host favourable landing platforms for targeted integration of transgenes encoding coagulation factors or antibodies.

**4:45 Genome Editing, NGS, microRNAs and Beyond: Transforming New Technologies into More Efficient CHO-K1 Manufacturing Cell Lines**

*Simon Fischer, Ph.D., Head, Cell Line Development CMB, Boehringer Ingelheim Pharma GmbH & Co. KG*

Genome editing, next-generation sequencing (NGS) and cell line engineering using microRNAs (miRNAs) have emerged as key technologies towards successful biopharmaceutical process development. We have evaluated and integrated these tools into our state-of-the-art cell line development and characterization processes in order to enhance manufacturing of innovative protein therapeutics. This talk will summarize our recent achievements in using these technologies and thus present novel solutions for future challenges in bioprocessing.

**5:15 TapBoost® Technology: Enhanced Protein Production by Improved Protein Folding System**

Sponsored by SOLA BIOSCIENCES

*Akinori Hishiya, Ph.D., Principal Scientist, Co-Founder, Biology, SOLA BioSciences*

Therapeutic recombinant proteins produced using mammalian expression systems often have misfolding issues. We have developed a novel technology called TapBoost® technology, which assists proper protein folding systems specifically for a targeted protein. TapBoost® has enhanced the production of many therapeutic recombinant proteins including monoclonal antibodies and Fc fusion proteins.

**6:00 – 9:00 Recommended Dinner Short Course***

**SC9: Transient Protein Production in Mammalian Cells**

** Separate registration required, see page 6 for details.*

## FRIDAY, AUGUST 25

**8:00 am Registration Open and Morning Coffee**

## GLYCOSYLATION

**8:25 Chairperson's Remarks**

*Richard Altman, MS, Scientist V, Protein Technologies, Amgen*

**8:30 Cell-Based Glycoengineering of Biologics**

*Claus Kristensen, Ph.D., Associate Professor, Cellular and Molecular Medicine, Copenhagen Center for Glycomics, University of Copenhagen*

Glycan structures are important for efficacy of glycoprotein therapeutics. Glycodisplay have developed a cell based platform to display different glycan structures on drug candidates for optimization. We apply targeted cell engineering to generate large panels of glycoengineered cell lines with different glycosylation capacities. By expressing a drug candidate protein in a panel of our cell lines, we can produce glycovariants of the protein for screening

and identification of novel glyco-optimized lead. Applications of our GlycoDisplay technology will be presented.

**9:00 Strategies for the Control of Glycosylation during the Production of a Recombinant Protein**

*Michael Butler, Ph.D., Distinguished Professor Emeritus, University of Manitoba, and CSO, Cell Technology, National Institute of Bioprocessing Research & Training (NIBRT)*

Glycosylation is an important post-translational process that leads to heterogeneity of recombinant proteins. This heterogeneity affects the biological activity and clinical efficacy of these bioproducts. The challenge in a bioprocess is to control the heterogeneity to ensure consistency and a profile that maximizes the desired biological properties. The profile can be controlled by cellular glycoengineering, media manipulation or enzymic re-modelling during the downstream process. Possible strategies for the use of each of these methods will be shown for the production of an antibody.

**9:30 Optimization and Control of Human Glycosylation during Biotherapeutic Development**

*Rainer Stahn, Ph.D., Director, Process Development, Glycotope GmbH*

A glycoengineered human production platform for the production of human biopharmaceuticals was generated. Based on this technology high yield production of, e.g., mAbs, bispecifics, blood factors and hormones with optimized human glycosylation was established. Aspects of controlling and optimizing glycan structures will be presented at different stages of development as cell line development or process development. Additionally, we present state-of-the-art tools for glycan analysis. Additionally, state of the art tools for glycan analysis will be presented, which is a foundation for rapid and efficient cell line and process development.

**10:00 Networking Coffee Break**

## GLYCOSYLATION & CLONE SELECTION AND OPTIMIZATION

**10:30 Investigating Alterations in the CHO N-Glycome Following Exposure to Leachables from Single-Use Bioreactors**

*Jonathan Bones, Ph.D., Principal Investigator, Characterization and Comparability Laboratory, National Institute for Bioprocessing Research and Training (NIBRT)*

The cellular N-glycome of CHO cells, characterized using two dimensional liquid chromatography with high resolution mass spectrometry, is highly complex, consisting of a dominant high mannose series and a broad range of complex N-glycans bearing varying degrees of sialylation and poly-lactosamine motifs. The dynamics of the CHO N-glycome is described following exposure to leachable compounds from single use bioreactors. Correlation with product quality attributes, including mAb glycosylation, were also investigated.

**11:00 From Thousands of Clones to the Final One**

*Dattananda Chelur, Ph.D., Lab Head, Cell Line Development, Integrated Biologics Profiling (IBP)/ BTDM, Novartis Institutes for BioMedical Research, Inc.*

CHO cells are the most widely used host for large-scale production of recombinant therapeutic proteins. In order to identify the most suitable lead cell lines, Novartis started to introduce a development process that comprises thorough early candidate profiling focusing on biophysical properties of candidates, followed by a cell line development process applying an efficient selection strategy in combination with process-tailored automation for clone imaging, clone handling, and selection.

**11:30 FACS-Based Clone Selection and Host Cell Engineering to Improve the Production and Quality of Recombinant Proteins in CHO Cells**

*Elizabeth Scheideman, Ph.D., Director, Cell Line Development, Vaccine Production Program, Vaccine Research Center, National Institutes of Health (NIH)*

We have been working towards improving our clone selection process and assurance of clonality through the development of a FACS-based platform for single cell cloning, which involves optimization of sorting conditions, medium development, and work on novel reporter-based systems for sorting mAb and especially non-mAb targets. In addition, we are working on methods of modifying our host cells to improve product quality attributes and working to incorporate these metrics earlier in our clone selection process.

**12:00 pm Sponsored Presentation** *(Opportunity Available)*

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

**1:15 Session Break**

## INNOVATING CELL LINE DEVELOPMENT

**1:25 Chairperson's Remarks**

*Jonathan Bones, Ph.D., Principal Investigator, Characterization and Comparability Laboratory, National Institute for Bioprocessing Research and Training (NIBRT)*

**1:30 BESTcell: Fast Cell Line Development for CHO Clones with High-Yield Protein Production Using Euchromatin-Containing BAC Expression Vectors**

*Anton Bauer, Ph.D., COO, The Antibody Lab GmbH*

Upon stable cell line generation, chromosomal integration site of the vector DNA has a major impact on transgene expression. By using chromosomal loci in BACs and random integration into host cell chromosomes, we developed stable high-yield production cell lines at an unprecedented speed. We performed several case studies for CHO production clones, and we established for antibodies and even difficult-to-express proteins generation of production clones within 3 weeks from transfection.

# Optimizing Cell Line Development

Enhancing Expression



**2:00 Optimizing CHO Cell Culture Process through Mechanistic Understanding of Cysteine Capping Modifications for Improving Site-Specific ADCs**

*Xiaotian Zhong, Ph.D., Senior Principal Scientist/Lab Head, Pfizer BioTherapeutic Research*

Cysteine (Cys)-based site-specific ADCs allow for a rapid and simple chemical conjugation reaction to attach diverse linkers/ payloads to provide homogeneous ADC products. This presentation will describe a novel discovery on Cys residue's post-translational modification in stable CHO cells. The so-called Cys-capping modification utilizes a mechanism that is different from the conventional oxidoreductase-mediated process for protein disulfide formation. The unexpected discovery has led to a novel and highly efficient CHO cell culture process for improving protein therapeutics conjugation.

**2:30 A Novel Preclinical *in vivo* Mouse Model for Malignant Brain Tumor Growth and Invasion**

*Purna Mukherjee, Ph.D., Research Assistant Professor, Biology, Boston College*

Glioblastoma multiforme (GBM) is a rapidly progressive disease of morbidity and mortality and is the most common form of brain cancer in adults. Lack of appropriate *in vivo* models has been a roadblock to developing effective therapies for GBM. A new highly invasive *in vivo* GBM model is described that was derived from a spontaneous brain tumor (VM-M3) in the VM/Dk inbred mouse strain. The VM-M3 cells are labeled with the firefly luciferase gene allowing detection through bioluminescent imaging.

**3:00 Mito-ID Based Mitochondrial Membrane Potential Staining: A Screening Strategy for Cell Line Development Clone Selection**

*Lina Chakrabarti, Ph.D., Scientist, Cell Culture and Fermentation Sciences, Medimmune, Inc.*

Using clonal cell lines and pools from cell line development projects, we performed a series of experiments to evaluate mitochondrial membrane potential (MMP) with Mito-ID dye and found that the intensity of MMP fluorescent signal correlated with the titer values from the producer clones. We also determined that cell sorting based on high MMP staining could potentially combine the two steps of cloning and enriching for high producer cells.

**3:30 End of Conference**

Register Online!

BioprocessingSummit.com

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

# Downstream Processing

Downstream processing is an area ripe for technology innovations. The need to meet high upstream titers and the demand for lower cost are pushing companies to look at more creative strategies in downstream, giving rise to new trends like Continuous Processing, Advances in Purification Technologies, as well as improved techniques for Virus and Pathogen Clearance and Safety in Biologics. The weeklong Downstream Processing stream will highlight the latest developments in these three respective fields.

2017 DOWNSTREAM PROCESSING TRACKS

**AUGUST 21-22**
AGENDA Continuous Processing in Biopharmaceutical Manufacturing

**AUGUST 23-24**
AGENDA Advances in Purification Technologies

**AUGUST 24-25**
AGENDA Virus & Pathogen Clearance & Safety in Biologics

## MONDAY, AUGUST 21

**8:00 am Short Course Registration Open**

**9:00 – 11:30 Recommended Morning Short Courses***

**SC3: Advanced Process Control, Intensified DoE and Hybrid Modeling for Process Optimization and Characterization**

** Separate registration required, see page 6 for details.*

**11:30 Main Conference Registration Open**

## KEYNOTE PRESENTATIONS

**1:00 pm Chairperson's Opening Remarks**
*Richard D. Braatz, Ph.D., Edwin R. Gilliland Professor of Chemical Engineering, Massachusetts Institute of Technology*

**1:10 Model-Based Multivariate Monitoring and Control of QbD-Compliant Quasi-Continuous Integrated Pharmaceutical Production**
*Reiner Hans Luttmann, Ph.D., Professor, Bioprocess Automation, Bioprocess Engineering, Hamburg University of Applied Sciences*

This presentation includes the description of advanced data processing in a fully automated integrated production plant, consisting of a two step upstream followed by a four-step downstream line with cell clarification, removal of particles with micro-filtration as well as product concentration and purification with ultra-filtration and chromatography. Recursive production strategies are developed where a cell breeding, the protein production and the whole downstream line is operated both in series and in parallel. However, each main operation is shifted by one day. As a demonstration process, the production of potential Malaria vaccines with *Pichia pastoris* is intensively investigated. The production process is global observable and QbD compliant developed. This includes also process optimization with fully automated DoE-plants and the establishment of design spaces and control spaces.

**2:15 Continuous Manufacturing for National Preparedness & Response**

*Kimberly Sciarretta, Ph.D., Health Scientist, Division of CBRN Countermeasures, Biomedical Advanced Research & Development Authority (BARDA), Office of Asst Secretary for Preparedness and Response (ASPR), U.S. Department of Health and Human Services (HHS*

*Sau (Larry) Lee, Ph.D., Deputy Director (Acting), Office of Testing & Research [OTR], Office of Pharmaceutical Quality [OPQ], Center for Drug Evaluation & Research [CDER], U.S. Food & Drug Administration [FDA]*

Within the U.S. Department of Health & Human Services, the Food & Drug Administration (FDA) and the Biomedical Advanced Research & Development Authority (BARDA) have a collaboration around exploiting innovations in continuous manufacturing for the rapid response to chemical, biological, radiological & nuclear threats and/or reduce the costs with cGMP production of clinical scale batches.

**2:45 Refreshment Break**

## DRIVERS AND TECHNOLOGIES ENABLING CONTINUOUS BIOMANUFACTURING

**3:15 Continuous Bioprocessing: Enabling Technologies and Technology Needs**
*Karol Lacki, Ph.D., Chief Consultant, Karol Lacki Consulting AB*

A continuous process for manufacture of a biological product will rely on successful conversions of established batch operations into continuous operations and on implementation of new technologies specifically developed with continuous bioprocessing in mind. However, it will require a higher level of process understanding and process control. To reach this level of understanding and operational robustness, many technological and operational challenges will need to be addressed. This talk will discuss these challenges.

**3:45 Poster Highlight: Streamlining & Standardizing Direct Material Change Assessments in Biopharmaceutical Manufacturing.**
*Jia Liu, Ph.D., Scientist, Global Biologics MSAT, Genentech, Inc.*

Understanding and controlling direct materials is essential to understanding and controlling variability in biopharmaceutical manufacturing. Furthermore, Health Authorities require biopharmaceutical manufacturers to have oversight of the direct material suppliers and manage changes in compliance with cGMP. When changes to direct materials by suppliers occur, careful assessment is required to ensure there is no impact to process performance or critical quality attributes. Multiple departments are often required to collaborate on an assessment for a direct material change and the work load can quickly escalate considering the number of potential changes on hundreds of direct materials used in manufacturing. This presentation summarizes the recent efforts made at Roche/Genentech to streamline the assessment procedure impacting the entire biologics manufacturing network of the company and standardize the requirements (testing, data, etc.) to support change approval.

**4:00 How to Engage with Regulatory Agencies on Continuous Manufacturing**
*Stephanie Krogmeier, Ph.D., Senior Director, Global Regulatory Affairs, Vertex Pharmaceuticals*

The interest in continuous manufacturing in the pharmaceutically industry has grown significantly due to multiple advantages including improvements in flexibility, reliability and quality. However, concerns over technical, operational, and regulatory issues still remain. A critical component of successfully implementing continuous manufacturing is engagement with regulatory agencies. This session will discuss key approaches to successful health authority engagement as well as key learnings and examples from recent FDA and EMA interactions.

**4:30 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.

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

**7:00 Close of Day**

## TUESDAY, AUGUST 22

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

## PAT, PROCESS MODELING AND REAL-TIME, ONLINE MONITORING

**7:55 Chairperson's Remarks**
*Karol Lacki, Ph.D., Chief Consultant, Karol Lacki Consulting AB*

**8:00 FEATURED PRESENTATION: Process Modeling and Real-Time Control for On-Demand, Continuous Biomanufacturing**
*Richard D. Braatz, Ph.D., Edwin R. Gilliland Professor of Chemical Engineering, Massachusetts Institute of Technology*
This presentation describes the construction of process models and their application to the real-time control of biologic drug production in a small-footprint biomanufacturing platform. An opportunity is the use of a "virtual" plant for the dynamic operations of the entire end-to-end biomanufacturing process. The virtual plant can guide the selection of a control strategy for each critical quality attribute (CQA), design of startup and shutdown operations, and control systems design.

**8:30 Enabling Continuous Manufacturing through Data Science, Modelling and Advanced PAT Tools**
*Christoph Herwig, Ph.D., Head of Research Area Biochemical Engineering, Institute of Chemical Engineering, TU Wien, Vienna, Austria*
Continuous manufacturing (CM) is more than the continuous operation of individual process steps. CM needs strategies to link the process steps and to account for variations of the preceding step by the establishment to robust control strategies. This contribution provides structured approaches for gathering process understanding for integrated processing, providing this knowledge in the form of target oriented minimum models as well as real time solutions to enable model predictive control.

**9:00 Process Controls, Predictive Models and Right-Time Release in Biologics Drug Substance Manufacturing**
*Steven H. Doares, Ph.D., Vice President, Global Manufacturing Sciences, Biogen*
Biogen is implementing an end-to-end process control strategy for new biologics drug substance manufacturing, with a goal to significantly reduce process variability and potential batch failures. Under this control strategy, raw material impact is well understood through process characterization studies, and RMs for manufacturing are well understood through characterization testing and linked genealogies. Biogen also uses rapid analytical technologies to assess PQAs at the earliest possible intermediate steps ("right-time" testing).

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

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

**10:30 Continuous Online Monitoring and Feedback Control Using PAT Tool, Raman Spectroscopy for mAb Perfusion Process**
*Nikhil Ramsubramaniam, Ph.D., Senior Scientist, Upstream Processing, Bioprocess Technology & Expression, Merck & Co.*
Application of Raman spectroscopy as a process analytical technology tool for glucose monitoring and feedback control in an antibody perfusion process will be presented. An interval Partial Least Squares Regression model for glucose was developed wherein perfusion process parameters were changed in a stepwise manner. Implication of glucose feedback control at < 0.5 g/l in the bioreactor on cell culture, achieved by real-time Raman glucose prediction, will be discussed.

**11:00 Micro/Nanofluidic Approaches for Continuous Processing and Monitoring of Biologics**
*Jongyoon Han, Ph.D., Professor, Department of Electrical Engineering and Computer Science and the Department of Biological Engineering, MIT*
Ideas from microfluidics can be employed in all these aspects of biomanufacturing to significantly enhance the overall productivity, as well as the efficacy and safety of the final products. In this talk, I will showcase several examples, including microfluidic cell sorting utilized for advanced cell retention system for perfusion bioreactors, as well as nanofluidic system for continuous-flow multi-variate protein analysis for real time critical quality assessments.

**11:30 Validating a Commercial Manufacturing Process Control System Supporting PAT and RTRT**
*Michelle Bailey, Associate Director, GMP Operations, Continuous Manufacturing & Automation Validation, Vertex Pharmaceuticals, Inc.*
The pharmaceutical industry is adopting continuous manufacturing models to drive efficiency and higher quality. These new technologies require effective approaches for validation. This presentation discusses challenges encountered and approaches taken to validate PAT for in-process control and real time release testing with an emphasis on determining a validation strategy and taking validation from the lab to the plant.

*Sponsored by*

**12:00 pm Continuous Chromatography and Its Role in Process Intensification**
*Liselotte Molander, Senior Global Product Manager, GE Healthcare Life Sciences*
Focus on process intensification and increased process control continues in the biopharmaceutical industry. One key driver is reducing production costs while maintaining product quality and throughput. Approaches such as continuous chromatography has potential to increase chromatography resin capacity utilization, reduce equipment footprint and resource consumption. This presentation will cover periodic counter current chromatography in and beyond affinity chromatography mAb capture applications. We will also review a process economy tool to assess impact/cost as well.

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

**1:15 Dessert Refreshment Break in the Exhibit Hall with Poster Viewing**

## IMPLEMENTING CONTINUOUS PROCESSES

**1:55 Chairperson's Remarks**
*Steven H. Doares, Ph.D., Vice President, Global Manufacturing Sciences, Biogen*

**2:00 Intensification of a Multi-Product Perfusion Platform through Medium and Process Development**
*Andrew Chang, MSc, Principal Research Engineer, CMSC, Biopharmaceutical Development, Sanofi*
The talk will detail perfusion case studies on pushing to high productivity and low perfusion rate, the application of a standardized approach to different biologics, and engineering and economic considerations for commercial scale.

**2:30 Design Considerations for Implementation of a Continuous Chromatography Step into a Platform Purification Scheme**
*Rebecca Chmielowski-Wright, Associate Principal Scientist, Protein Purification, Merck & Co.*
In this presentation, we evaluated a three versus four column periodic counter-current chromatography (3C-PCC versus 4C-PCC) to replace the Protein A affinity batch mode purification step. Metrics included ≥ 85% step yield, productivity increase of ≥ 2-fold, resin cost reduction by ≥ 25%, and comparable product quality to the batch mode process. The challenges and differences in scale and operation between 3C-PCC versus 4C-PCC will also be presented.

**3:00 Integrated Continuous Manufacturing Progress and the Life Sciences Industry "Fad or Reality"**
*Robert Dream, Ph.D., Managing Director, HDR Company LLC*
Over the past decade, there have been significant advancements in science and engineering to support the implementation of continuous biopharmaceutical manufacturing. These investments along with the adoption of the QbD paradigm for biopharmaceutical development and the advancement of PAT for designing, analyzing, and controlling manufacturing have progressed the scientific and regulatory readiness for continuous manufacturing. The regulatory supports the implementation of continuous manufacturing using science- and risk-based approaches.

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

## SCALING UP OF CONTINUOUS PURIFICATION PROCESS

**4:15 3D Structure of Protein Precipitates and Fractal Dimension for Scale-Up of Continuous Precipitation**
*Alois Jungbauer, Ph.D., Professor, Department of Biotechnology, University of Natural Resources and Life Sciences, Austrian Centre of Industrial Biotechnology (ACIB), Austria*
The 3D structure of protein precipitates is still widely unknown, especially the implications of different precipitate structures on possible downstream applications for purification. We use wide field microscopy and cryo-TEM to visualize the structure of PEG precipitates. Lab and pilot scale precipitation have concluded that in continuous precipitation with reactors with narrow residence time distribution such as tubular reactors, it is not necessary to operate at steady state as confirmed by the fractal dimension of the precipitate flocs.

**4:45 Development of a Continuous Purification Process for mAb and Scale-Up Exercise**
*Xavier Le Saout, Associate Manager, Biotech Process Sciences Technology & Innovation, Global Manufacturing & Supply, Merck Serono SA*
To fulfil future bioprocess manufacturing requirements, innovation is key. A lot of intensifying DSP tools are in development and sometimes close to implementation as multi columns system, SPTFF or continuous operations. This presentation will cover most of these tools, highlighting their main advantages, limitations and their potentials for manufacturing implementation. Finally, cases studies using integrated DSP platform and platform scale-up will be discussed.

**5:15 Close of Conference**

**6:00 – 8:30 Recommended Dinner Short Course***
**SC6: Integrated Continuous Biomanufacturing - An Implementation Approach: Planning, Technology, Regulatory, and Manufacturing Advantages to Present Robust Optimized Batch Manufacturing**
** Separate registration required, see page 6 for details.*

## WEDNESDAY, AUGUST 23

**7:00 am Registration Open and Morning Coffee**

**8:05 Chairperson's Opening Remarks**
*Stefano Menegatti, Ph.D., Assistant Professor, Department of Chemical and Biochemical Engineering, NC State University*

**8:15 KEYNOTE PRESENTATION:**
**Protein Engineering and Evolving Demands in Protein Purification: A Critical Appraisal of Workflow Options in Downstream Processing**
*David O'Connell, Ph.D., Lecturer in Biotherapeutics, School of Biomolecular & Biomedical Science, University College Dublin*
This presentation will review the area of purification of fusion proteins, antibody fragments, gene therapies, and virus and vaccine therapies, and feature case studies highlighting innovative approaches to their improved recovery.

## PURIFICATION OF NOVEL FORMATS

**9:00 Downstream Process Development of an *in vivo* Radiolabeled Protein Diagnostic Expressed in *E. coli***
*Brian O'Mara, Senior Scientist, Bioprocess Development, Bristol-Myers Squibb*
Standard pathological diagnostic applications utilize immunohistochemistry (IHC) techniques to detect specific tumor associated antigens of biopsied tissues using antibodies labeled with a reporter molecule. The usefulness of IHC as a diagnostic tool is limited by the small sample size of the biopsy which may either miss or underestimate the extent of the disease. Here we discuss the process development of an *E. coli* expressed radiolabeled protein conjugate used for the *in vivo* diagnosis of a specific tumor antigen.

**9:30 Purification of Common Light Chain IgG-Like Bispecific Antibodies Using Highly Linear pH Gradients**
*Beth Sharkey, Associate Scientist, High Throughput Expression, Adimab, LLC*
This talk will demonstrate an approach to producing bispecific antibodies that deviates from the strategy of introducing potentially undesirable mutations to enable manufacturing. Instead, a high resolution purification method is leveraged to generate a panel of entirely native common light chain bispecific antibodies. The technique is compatible with ion exchange resins that are suitable for industrial scale applications and can be used for other bispecific antibody formats as well.

**10:00 Coffee Break in the Exhibit Hall with Poster Viewing**
*Sponsored by* ROCKLAND antibodies & assays

## TECHNOLOGY ADVANCES AND NEW APPROACHES IN DOWNSTREAM PROCESSING

**10:45 Advances and New Approaches in Affinity Chromatography**
*Krunal Mehta, Ph.D., Scientist, Purification Process Development, Amgen*
The high cost of Protein A resins has required better utilization of its capacity or the use of cheaper and comparable alternatives to improve the downstream process economics. While the improvements in capacities have been limited, achieving higher operational flow rates has led to much more dramatic improvements in the productivity of Protein A capture step. The significantly higher productivity through substantially reduced cycle times enables better resin utilization and reduces the resin requirements without compromising the throughput of the capture step.

**11:15 Leveraging Affinity Capture to Also Select Critical Quality Attributes**
*Warren Kett, Ph.D., CSO, Avitide, Inc.*
The challenges of purification are magnified when not only removal of host-derived impurities is difficult, but product related impurities also persist. We present case studies where we developed affinity resins for biopharmaceutical companies that met both goals - a single affinity column that provided robust capture and also selected the correct product isoform. In addition to the obvious advantages of these dual functional resins, unforeseen process benefits also accrued.

**11:45 A Novel Chromatographic Technology: Enhancing Performance Utilizing a Modular Lattice Supported Resin Bed**
*Sponsored by* JSR Life Sciences
*Masayoshi Nagaya, Global Technology Manager, Separation Science Group, JSR Life Sciences*
Improvements in chromatography utilization have been focused mostly on resin design, buffer selection and operating modes. A novel technology that allows full bed support via a 3D printed internal lattice enables modular chromatography, prepacked ease of use and enhanced productivity. Data will be shown to illustrate productivity improvement of several fold for a Protein A capture step.

**12:15 pm Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

**1:00 Session Break**

**1:45 Chairperson's Remarks**
*David O'Connell, Ph.D., Lecturer in Biotherapeutics, School of Biomolecular & Biomedical Science, University College Dublin*

**1:50 Evaluation of Straight-Through Protein Chromatography to Enable Truly Continuous Bioprocessing**
*Stefano Menegatti, Ph.D., Assistant Professor, Department of Chemical and Biochemical Engineering, NC State University*
We have developed a technology that integrates proteomics tools with statistical-graphical methods to (1) determine the clearance of HCPs and (2) identify complementary technologies for HCP removal. To demonstrate, we evaluated the ability of commercial chromatographic resins to remove HCPs from CHO-S supernatants. We have derived statistical correlations between % removal of each protein species and its isoelectric point, and identified 24 HCPs that were not removed by any of the resins studied.

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# Advances in Purification Technologies

**2:20 Development of Next Generation mAb Purification Process**
*Tingting Cui, Ph.D., Scientist II, Purification Process Sciences, MedImmune*
This case study demonstrates a systematic approach to adopt a 'flow through' process in designing purification of a mAb with high titer. As a result, the new downstream process enhances the process productivity by 3- fold, significantly reduces buffer volumes by 10 fold and secures the product quality. This type of downstream process could be utilized for other potential high titers biotherapeutics.

**2:50 Advances in Harvest Technologies**
*Glen Giese, Scientist, Group Leader, Purification Development, Genentech, Inc.*

**3:20 Efficient Devices for Process-Scale Chromatography**
*Raja Ghosh, Ph.D., Professor, Canada Research Chair in Bioseparations Engineering, Chemical Engineering, McMaster University*
This presentation focuses on a radically different approach of using a cuboid or "box-shaped" packed-bed instead of a "column". The design of such a cuboid packed-bed is inspired by that of a laterally-fed membrane chromatography device, also developed by the presenter. The workings of such devices, and how they could potentially play an important role in process-scale chromatography, are explained.

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

**4:45 PLENARY KEYNOTE PRESENTATION**
*(See page 3 for details.)*

**6:00 Networking Reception in the Exhibit Hall with Poster Viewing**

**7:00 Close of Day**

## THURSDAY, AUGUST 24

**8:00 am Registration Open and Morning Coffee**

## IMPROVING DOWNSTREAM PROCESS EFFICIENCIES

**8:25 Chairperson's Remarks**
*Raja Ghosh, Ph.D., Professor, Canada Research Chair in Bioseparations Engineering, Chemical Enginering, McMaster University*

**8:30 Buffer Concentrates: Improving Downstream Efficiency through Real-Time Monitoring, Release and Control**
*Veronica Adams, MSc, Engineer II, Process Biochemistry, Biogen*
Two strategies which can increase efficiency in buffer preparation and storage include real time monitoring of buffer characteristics during preparation and the use of buffer concentrates. Real time monitoring via inline pH and conductivity probes during buffer preparation and release can streamline preparation, reducing offline sampling for buffer release. Buffer concentrates can alleviate the volume requirements for increased buffer usage, reducing the storage footprint required.

**9:00 BioXcellence Tech Transfer Concept – An Insight in General Tech Transfer Approach Including BI's Quality Culture Initiative**
*Daniel Kronberger, MSc, Head of Downstream Pilot, Process Sciences, Boehringer Ingelheim RCV GmbH & Co. KG*
The talk will mainly focus on BI's tech transfer concept, showing the whole engineering procedure from process science to production scale. Working with microbial expression systems often means dealing with very complex purification processes. Achieving an efficient, fast and highly productive purification process within a short timeline requires an accurate communication strategy of process science and full scale production engineers. This cooperation follows well established documents and meeting culture.

**9:30 Presentation to be Announced** *Sponsored by* C Technologies, Inc.

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

## HOST CELL PROTEINS REMOVAL/ REDUCTION IN DOWNSTREAM PURIFICATION

**10:45 Tales from the Crypt: The Hidden Consequences of Cell Death on Downstream Processing**
*Pete Gagnon, MSc, President and CSO, Validated Biosystems*
This presentation will show the most damaging species of host cell proteins consisting of mixed covalent and non-covalent associations among chromatin remnants and misfolded proteins including product-related impurities. It will trace their development from normal living cell metabolism, through apoptosis, secondary necrosis, and continuing in cell culture supernatants. It will highlight the primary mechanisms by which they interfere with purification methods and finally touch on methods for suspending their adverse effects.

**11:15 Use of Activated Carbon as an Adsorbent in the Polishing Step**
*Romas Skuda, Ph.D., Senior Scientist, Chromatography, Biopharm Process Solutions, Merck KGaA*
We will present case studies showing flow-through purification results in the effective separation of HCPs, antibody fragments and LMW substances from post Protein A affinity capture solutions. In most cases, the mAb recovery was >85% and HCP amount was reduced to <10ppm. This technology can be adapted to standard and new purification templates while maintaining critical product quality attributes and could enable fully continuous operation by linking the different flow through chromatography media to form a single integrated system.

**11:45 Optimize Host Cell Protein Reduction in Downstream Processes with the Aid of LC-MS Technique**
*Yinying Tao, Ph.D., Senior Research Scientist, Eli Lilly*

**12:15 pm Enjoy Lunch on Your Own**

**1:15 Dessert Refreshment Break in the Exhibit Hall and Last Chance for Poster Viewing**

**1:55 Close of Conference**

# Virus and Pathogen Clearance and Safety in Biologics:

Detection, Clearance, Risk Mitigation and Management

## THURSDAY, AUGUST 24

**11:30 am Registration Open**

**12:15 pm Enjoy Lunch on Your Own**

**1:15 Dessert Refreshment Break in the Exhibit Hall and Last Chance for Poster Viewing**

## RISK MANAGEMENT, STRATEGIES & CASE STUDIES

**2:45 Viral Safety Testing of Insect Cells for Production of Influenza Vaccines**

*Penny Post, Ph.D., Vice President, Protein Sciences Corporation*

This presentation talks about uses of the baculovirus expression vector system and insect cells to produce novel vaccines. The baculovirus expression system technology provides advantages of speed, cost, and safety. Our recombinant seasonal influenza vaccine Flublok® was FDA approved in 2013, making this product the world's first approved recombinant influenza vaccine. This talk will describe our virus safety testing strategy for our novel expresSF+® insect cell line.

**3:15 Process Control Strategy for Gene Therapy Products**

*Mark Plavsic, Ph.D., CTO, Lysogene*

A good process control is important for the successful development of the gene therapy products. In this presentation, we will discuss the importance processes in gene therapy based product and design of a good process control strategy.

**3:45 Comparison and Trend Analysis of Virus Retentive Filter Performance in Viral Clearance Studies**

*Kitti Neumann, Senior Manager, Process Evaluation, Charles River Laboratories*

Given current industry expectation for virus retentive filtration, viral clearance study results have been evaluated for specific performance trends over time. Based on Charles River database information dating back to 2014, this virus removal capacity has been evaluated, with a focus on filtration results obtained for selected filter vendors. In addition, this trend analysis will include reference to study design elements that have influenced these results.

**4:00 Refreshment Break**

**4:15 Industry Approaches to Facility Segregation for Viral Safety**

*Paul Barone, Associate Director, BioMAN and CAACB, MIT Center for Biomedical Innovation*

The Consortium on Adventitious Agent Contamination in Biomanufacturing (CAACB) has begun a project with the following goals:

- Define "pre- and post-viral clearance zones" and "pre- and post-viral clearance materials"
- Define "functionally closed" manufacturing systems
- Identify an array of facility segregation approaches used for the safe and effective production of recombinant biologics as well as plasma products

This presentation will discuss the results of this collaborative endeavor to date.

**4:45 PANEL DISCUSSION: Impact of Alternative Cell Lines and Human Cell Lines on Viral Safety**

*Moderator:*

*Mark Plavsic, Ph.D., CTO, Lysogene*

*Panelists:*

*Barbara J. Potts, Ph.D., Senior Consultant, Potts and Nelson Consulting, LLC*

*Brad Stanley, Scientist II, Technical Development, Biogen*

*Penny Post, Ph.D., Vice President, Protein Sciences Corporation*

**5:15 Close of Day**

## FRIDAY, AUGUST 25

**8:00 am Registration Open and Morning Coffee**

## RAW MATERIALS SAFETY

**8:25 Chairperson's Remarks**

*Barbara J. Potts, Ph.D., Senior Consultant, Potts and Nelson Consulting, LLC*

**8:30 Raw Materials as the Source of Porcine Circovirus, Porcine Hepatitis E Virus and Mycoplasmas; Strategies to Prevent and Remove from Biologics**

*Barbara J. Potts, Ph.D., Senior Consultant, Potts and Nelson Consulting, LLC*

Strategies will be presented to prevent the contamination of biologics with porcine circovirus, porcine hepatitis E virus from contaminated porcine raw materials and from mycoplasmas found in peptones and bovine sera. Removal and inactivation methods will be presented that have been successful including a case study of porcine circovirus in pepsin.

**9:00 FEATURED PRESENTATION:**
**Management of Risks Associated with Animal Derived Materials**

*Rosemary J. Versteegen, Ph.D., CEO, International Serum Industry Association*

The International Serum Industry Association has several ongoing programs designed to help mitigate the risk of using animal-derived materials. This presentation will include:

- An introduction to ISIA
- An overview of the Serum market
- Things to consider when selecting a serum source
- Why traceability matters
- A description of key ISIA programs such as traceability, geographic origin, animal age, gamma irradiation

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# Virus and Pathogen Clearance and Safety in Biologics:

Detection, Clearance, Risk Mitigation and Management

## UPSTREAM & DOWNSTREAM PROCESSING AND PURIFICATION

**9:30 Leveraging Modular Claims for Viral Clearance**

*Brad Stanley, Ph.D., Scientist II, Technical Development, Biogen*

Extensive experience in performing validation studies and improvements in scientific understanding of viral clearance and inactivation mechanisms have facilitated the use of claims that rely less on molecule specific validation studies. Leveraging published ASTM standard practices for low pH virus inactivation and internal data demonstrating robustness of detergent inactivation and virus filtration across programs will be discussed as part of an integrated strategy to ensure viral safety.

**10:00 Networking Coffee Break**

**10:30 Evaluation of Low pH Viral Inactivation and Viral Filtration Data from Multiple Company Collaboration**

*Xinfang Li, Principal Scientist, Process Science and Engineering, ImmunoGen, Inc.*

Considerable resources are spent within the biopharmaceutical industry to perform viral clearance studies which are conducted for widely used unit operations that are known to have robust and effective retrovirus clearance capability. The collaborative analysis from the members of BioPhorum Development Group Viral Clearance Working Team considers two common virus reduction steps in biopharmaceutical processes: low pH viral inactivation and viral filtration.

**11:00 Viral Clearance Prediction through the Use of a Non-Infectious MVM-Virus Like Particle**

*David Cetlin, Founder & CEO, MockV Solutions LLC*

Due to the infectious nature of live viruses, viral clearance "spiking studies" are typically conducted in specialized BSL-2 facilities at CROs. The costs and logistics associated are major hurdles during downstream process development activities. A non-infectious Minute Virus of Mice - Virus Like Particle (MVM-VLP) was generated for use as an economical spiking surrogate. Discussed here are the results from a side by side MVM vs. MVM-LVP nanofiltration spiking study.

**11:30 Isolation and Characterization of Virus-Free Insect Cell Lines for Baculovirus-Mediated Recombinant Protein Production**

*Donald Jarvis, Ph.D., Professor, Molecular Biology, University of Wyoming*

Insect cell lines most commonly used as hosts for baculovirus-mediated recombinant protein production, derived from Trichoplusia ni (Tn) and Spodoptera frugiperda (Sf), are commonly contaminated with adventitious viral agents. The Tn contaminant was identified as Tn cell line virus (TnCLV), whereas the Sf contaminant was identified as Sf-rhabdovirus (Sf-RV). In this talk, we will describe the isolation and characterizion of TnCLV- and Sf-RV-negative Tn and Sf cell lines, respectively.

**12:00 pm Sponsored Presentation** *(Opportunity Available)*

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

**1:15 Session Break**

## TOOLS FOR DETECTION OF EMERGING VIRUSES AND PATHOGENS

**1:25 Chairperson's Remarks**

*Cassandra Braxton, Ph.D., Scientist II, Quality Technology & Development, Biogen*

**1:30 Utilizing Next-Generation Sequencing and Rapid Molecular Methods to Advance Viral Detection in the Biopharmaceutical Industry**

*Cassandra Braxton, Ph.D., Scientist II, Quality Technology & Development, Biogen*

Viral safety is a critical aspect of ensuring the safety of biological products in the biopharmaceutical industry. Biogen is exploring next-generation sequencing as a novel approach to detecting non-specific adventitious viruses that may be introduced into bulk harvest material for biologic drug substance. This presentation will provide an overview of current practices for adventitious virus detection and technologies we are driving towards implementing in the future.

**2:00 Reference Materials for Adventitious Virus Detection by Metagenomics**

*Edward Mee, Ph.D., Senior Scientist, Live Viral Vaccines, Virology, National Institute for Biological Standards and Control*

High throughput sequencing offers great potential for improved adventitious virus screening, however several practical challenges exist, including cost, complexity and the difficulty in defining limits of detection for unknown viruses. Well-characterized reference materials containing representative virus genome, capsid and envelope structures will enable meaningful inter-laboratory comparisons, support method development and act as process run controls.

**2:30 Breakout Discussion**

**3:30 End of Conference**

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# Analytical & Quality

The weeklong Analytical & Quality stream offers in-depth updates on critical steps in biopharmaceutical development that impact product quality, safety and regulatory compliance. Separate meetings will focus on the detection, analysis and removal of host cell proteins, early stage analytical development and the implementation of process characterization and control strategies. Over fifty in-depth presentations will give attendees insight into the best practices being applied across the industry.

2017 ANALYTICAL & QUALITY TRACKS

**AUGUST 21-22**
AGENDA Host Cell Proteins: Detection, Analysis & Removal

**AUGUST 23-24**
AGENDA Early Analytical Development for Biotherapeutics

**AUGUST 24-25**
AGENDA Process Characterization & Control

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# Host Cell Proteins

Detecting, Analyzing and Removing Host Cell Proteins

## MONDAY, AUGUST 21

**8:00 am Short Course Registration Open**

**9:00 – 11:30 Recommended Morning Short Courses***

**SC2: Comparability Strategies for Cell and Gene Therapies**

** Separate registration required, see page 6 for details.*

**11:30 Main Conference Registration Open**

## RISK ASSESSMENT AND CONTROL STRATEGIES

**1:00 pm Chairperson's Opening Remarks**

*Carl Co, Ph.D., Senior Scientist, Biogen*

**1:10 A Holistic Phase Appropriate Strategy for HCP-Limits and HCP Characterization**

*Markus Haindl, Ph.D., Director, Development Analytics, Roche*

Increased usage of new technologies like Mass Spectrometry opens up entirely new strategic possibilities to test and characterize HCP – not only in purified Drug Substance to ensure patient safety but also for in-process samples to characterize downstream process performance. A smart and phase-appropriate combination of traditional assay formats with new technologies becomes key to support an IMP product during its development lifecycle until launch.

**1:45 Host Cell Protein Control Strategy Reassessment for a CHO-Derived Protein Therapeutic**

*John M. Rolf, Ph.D., Director, Corporate Product Quality, Amgen*

Immunoassay tests are standard to establish HCP impurity specifications and monitor protein therapeutic lot-to-lot consistency. However, multi-analyte Immunoassay tests may over- or under-quantify. In this case study, Mass Spectroscopy (MS) identified and quantified individual HCPs from protein product drug substance, comparing results to the Immunoassay. The case study demonstrates how MS testing (and supplemental characterization data) was used to redefine the HCP control strategy – without impacting product or patient safety.

## CLINICAL RELEVANCE OF HCPS

**2:15 Specific Immune Response to PLBL2, a Host Cell Impurity in Clinical Material**

*Melissa L. Cheu, Principal Scientific Researcher, BioAnalytical Sciences, Genentech, Inc.*

A product-related impurity was identified in material used in a clinical study. To assess the potential of patients developing an immune response to the impurity and the impact on immunogenicity of the therapeutic, two bridging ELISAs were developed and validated. Samples from subjects were evaluated in both assays. This presentation will discuss the results of the immunogenicity assessment to the impurity and observed immunogenicity rate of the antibody therapeutic.

**2:45 Refreshment Break**

## CURRENT CHALLENGES AND EXPECTATIONS

**3:15 Host Cell Proteins and Regulatory Expectations**

*Erika Friedl, Quality Expert, Haematology and Transfusion Medicine, Paul-Ehrlich Institute*

**3:45 Sponsored Presentation** *(Opportunity Available)*

**4:00 Obtaining EU-Wide (CHMP) Scientific Advice for HCP Issues**

*Ruth Paul, Independent Consultant*

I will share my experiences of working with the pharma industry to obtain EU-wide scientific advice on issues relating to HCP levels in biotech products. I will discuss the issues raised, the strategic advice that EMA/CHMP gave (in general terms) and highlight some of the potential pitfalls of the process from the company's perspective.

**4:30 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.

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

**7:00 Close of Conference**

## TUESDAY, AUGUST 22

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

**7:55 Chairperson's Remarks**

*Fengqiang Wang, Ph.D., Associate Principal Scientist, Merck Research Laboratories, Merck & Co. Inc*

**8:00 Reducing Host Cell Protein Burden by Molecular Design and Selection**

*Yiqing Feng, Ph.D., Research Fellow, BioTechnology Discovery Research, Eli Lilly and Company*

Removing host cell proteins has become a critical aspect of biopharmaceutical process development. It will be advantageous to design and select therapeutic candidates that have reduced tendency for HCP association to make the removal easier during the purification process. We have explored the molecular attributes of monoclonal antibodies that contribute to HCP association which will be discussed in this presentation.

## HCP CHARACTERIZATION WITH MASS SPECTROMETRY

**8:30 Recent Case Studies of Identification and Quantification of Host Cell Proteins by Mass Spectrometry**

*Veronika Reisinger, Ph.D., Lab Head, Physico-Chemical Characterization, Novartis Technical*

LCMS/MS can be used as a complimentary method to ELISA for detection and monitoring of residual host cell proteins (HCP). A platform approach was established for CHO and *E. coli*-derived products to identify and relatively quantify HCPs. In the presented case studies, comparability exercises for two FDA-approved biosimilars are discussed.

**9:00 Increased Throughput and Accuracy in Host Cell Protein Quantitation Using Spectral Library Searches**

*Michelle Busch, Scientist, Bioanalytics Characterization, Sanofi*

A high throughput method was developed to identify and quantify residual host cell proteins (HCPs) throughout purification. A spectral library was created from manually verified peptides to increase the speed of data analysis and reduce error and false positive matches. The library search could then be utilized for subsequent experiments, allowing knowledge of the product and its HCPs to accumulate and not have to be discovered repeatedly.

**9:30 Vendor Neutral Host Cell Protein Detection and Reporting for LCMSMS Data**

*Sponsored by* PROTEIN METRICS

*St John Skilton, Ph.D., Senior Director, Global Sales and Marketing, Protein Metrics Inc.*

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

**10:30 Quantitative Investigation of Host Cell Protein Impurities: Bridging the Gap between ELISA and Orthogonal LC-MS/MS Analysis**

*Ying Zhang, Senior Scientist, Analytical Research & Development, Pfizer*

LC-MS/MS has emerged as an orthogonal approach to ELISA for analyzing HCPs, providing both qualitative and quantitative information on individual HCPs. Sample prep, method parameters, and different mass spectrometers were investigated. We found that the quantitative readouts between HCP-specific ELISAs and LC-MS/MS were quite comparable, permitting "real-time" targeted-HCP monitoring during process development and comprehensive HCP analysis for final purified drug substance.

**11:00 Identification and Quantification of HCPs in mAbs, Recombinant Proteins and Biosimilars by Mass Spectrometry**

*Sponsored by* CAPRION

*Laura McIntosh, Ph.D., Vice President Translational Research, Scientific Management, CAPRION BIOSCIENCES INC.*

Gel-free, label-free mass spectrometry (MS) enables identification and quantitation of total and individual HCP in biotherapeutic products, and represents an orthogonal method to ELISA. Examples will be presented showing use of semi-quantitative HCP discovery (LC-MS/MS) and absolute quantitation of HCP (LC-MRM/MS), as applied to monitoring of process changes/improvements, scale-up, batch uniformity, clearance, and comparison of Biosimilars vs Innovators. Caprion's HCP platform features customizable organism/process-specific databases, highly controlled analytical processes and reproducible robust detection (to ~1ppm).

**11:30 Navigating through the Challenges Encountered in Development of New HCP Reagents**

*Elise Levi, Associate Scientist III, Analytical Development, Biogen*

Generation of HCPs reagents takes up to a year and must therefore be methodically planned in order to meet process development and testing support deadlines. Unforeseen challenges may arise during the development of these reagents and require strategic decision making to meet project demands and support. In this talk, we present several case studies which highlight how we experimentally navigated through these challenges to make critical and timely decisions.

**12:00 pm Development of a Specific *E. coli* HCP ELISA based on Antibody Fragments**

*Sponsored by* BIOGENES

*Karsten Daehn, Senior Scientist, Immunoassay Development, BioGenes GmbH*

Biopharmaceuticals need to be free of contaminating HCPs prior to approval. For HCP determination of drug substances in early phases or during the DSP development commercial HCP-ELISAs are commonly used. In challenging cases special properties of the drug substance limit the use of full-length antibodies in ELISA, thus commercial HCP-ELISAs are not applicable during DSP development. BioGenes successfully overcame this issue by developing a specific *E. coli* HCP ELISA based on fragments of rabbit antibodies.

**12:30 Luncheon Presentation: New Strategies for Quality Control of Host Cell Protein Impurities**

*Sponsored by* charles river

*Olaf Stamm, Senior Specialist, Biological Testing Solutions, Charles River*

In this presentation we will show case studies from more than twenty year's experience in the field of HCP assay development. We will highlight critical parameter and quality attributes along the entire assay development process

**1:15 Dessert Refreshment Break in the Exhibit Hall with Poster Viewing**

## MANAGING CRITICAL REAGENTS AND COMMERCIAL PLATFORMS

**1:55 Chairperson's Remarks**

*Fengqiang Wang, Ph.D., Associate Principal Scientist, Merck Research Laboratories, Merck & Co. Inc*

**2:00 A Simple and Effective Conversion of an HCP Impurity Assay from Generic into Process-Specific**

*Bing Hu, Ph.D., CMC Analytical Sciences and Operations, Teva Biologics*

Per regulatory requirements, we made an assay conversion from a Cygnus generic to a process-specific HCP assay by replacing the assay standard with HCP proteins from Teva process-specific harvest, optimizing assay parameters including plate washing steps, and characterizing charactering the antibody's HCP coverage by 2D gel and western. In comparison with the generic assay, the process-specific HCP assay measured 40-60% more HCP impurity from GMP and engineering batches.

**2:30 Case Study: Qualifying an ELISA for HCP Quantification and Its Ability to Inform Purification Process Decisions**

*Samantha Kecman, Senior Analytical Development Associate, Pharmaceutical Sciences, Genocea*

ELISA is the most common method for HCP quantification. This presentation will cover aspects of anti-HCP ELISA assay development and qualification in the context of clinical-phase biopharmaceutical development. Discussion will include the generation and evaluation of anti-HCP antibodies against SF9 antigens using different animal systems and how quantification of HCPs from in-process samples can inform and influence purification process choices.

## MANAGING HCPS IN PROCESS DEVELOPMENT AND BY PRODUCT DESIGN

**3:00 Late Phase Process Development and Process Impurities Clearance – The Application and Optimization of HCP and Lipase Assays**

*Satish K. Sharma, Ph.D., Scientist II, Process Development Analytics, Bristol-Myers Squibb*

In a bioprocess development environment, HCP removal is essential in order to have a robust and safe commercial process. In a dynamic PD environment continuous process and method optimization is critical. Constant monitoring and risk assessment at early stage can minimize failure at late process development stage. Case studies and mitigation approaches that show correlation between HCP profile and specifically lipases will be discussed.

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

**4:15 Case Study: Clearance of an Immunogenic Host Cell Protein Impurity in a CHO-Derived Biotherapeutic Leading to a Standard Purification Approach**

*Ben Tran, Purification Development, Genentech, Inc.*

This case study highlights a specific CHO host-cell protein, Phospholipase B-like 2 (PLBL2). PLBL2 was isolated and identified from a clinical product during investigation of atypical “non-linear” sample dilution behavior in a multi-product CHOP ELISA. High-throughput screening and multivariate studies identified two modes of purification that effectively and robustly reduced PLBL2 levels. These screening tools have since been used to understand PLBL2 clearance and troubleshoot other co-purifying HCPs.

**4:45 PANEL DISCUSSION: HCP Moving Forward**

*Moderator: Fengqiang Wang, Ph.D., Associate Principal Scientist, Merck Research Laboratories, Merck & Co. Inc*

**5:15 Close of Conference**

**6:00 – 8:30 Recommended Dinner Short Course***
**SC5: Potency Assay Development for Cell and Gene Therapy Products**

** Separate registration required, see page 6 for details.*

# Early Analytical Development for Biotherapeutics

Optimizing Preclinical Analytical Development for Emerging Biotherapeutics

## WEDNESDAY, AUGUST 23

**7:00 am Registration Open and Morning Coffee**

**8:05 Chairperson's Opening Remarks**
*Darryl Davis, Ph.D., Associate Director, Biophysical Research and Analytical Development, Janssen Research & Development, LLC*

**8:15 KEYNOTE PRESENTATION:**

**Early Analytical Profiling to Facilitate Biologics Development**
*Tao He, Ph.D., Associate Research Fellow, BioMedicine Design, Pfizer, Inc.*

Early analytical profiling has become an integral component in biologics discovery & development. This presentation will highlight the recent technology development and their applications to facilitate selection and engineering of biologics leads. Approaches to minimize risk associated chemical degradation and other biophysical properties will be discussed.

## METHODS AND INSTRUMENTS

**9:00 Rapid Development of HPLC-UV Based Multiple Quality Attributes Method**
*Zhi Chen, Ph.D., Senior Scientist, Molecular and Analytical Development, Global Manufacturing & Supply, Bristol-Myers Squibb*

Transferability to QC is challenging for mass spectrometry (MS) based multiple quality attributes (MQA) methods. While HPLC-UV based peptide mapping methods can provide an alternative solution with potentially better accuracy and QC-friendly feature, the chromatographic separation of peptides of interest is not easy. In this presentation, the speaker will demonstrate case studies using HPLC modeling software and automation to facilitate rapid development of MQA methods.

**9:30 Multidimensional Chromatography Characterization of Drug Load Variants in a Thiol Linked Antibody-Drug Conjugate**
*Catherine Eakin, Ph.D., Principal Scientist, Seattle Genetics*

We developed three MS compatible 2D-LC methods for HT characterization of HIC peaks without manual fractionation. These methods are complementary and provide DAR confirmation by intact mass, identification of drug-load isomers and post-translational modifications by denaturing mass analysis, and localization of post-translational modifications to specific subunits by denaturing reduced mass analysis. Results demonstrate an efficient mechanism for characterization of ADC HIC peaks using multidimensional chromatography methods with in-line MS.

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

*Sponsored by* ROCKLAND antibodies & assays

**10:45 Integrated Development Environment for Production of Monoclonal Reference Material**
*Steven LaBrenz, Ph.D., Scientific Director, Cell and Developability Sciences, PDMS, Janssen R&D*

The focus on quality is primarily from the protein perspective. Quality however refers to both the raw materials and the product. There is a need to test the outcome (product quality and CQAs) alongside the impacting parameters (raw materials, formulation materials, process parameters). The concept of an integrated development environment (IDE), where the growth, formulation and analysis of the protein are performed alongside the analysis of the raw materials, is presented.

**11:15 Biophysical Characterization and Formulation Development of Live Viral Vectors as Vaccine and Immunotherapy Candidates**
*Ozan Kumru, Ph.D., Research Assistant Professor, Macromolecule and Vaccine Stabilization Center, University of Kansas*

Numerous live attenuated viruses and viral vectors are being developed as vaccine and immunotherapy candidates, yet their use can be challenging due to their inherent complexity and instability. Case studies will be presented in which various physical assays were used as part of formulation development to determine the extent of loss of viral particles due to environmental stresses and then compared to viral titer results.

**11:45 Analytical Method Toolbox for Biotherapeutics: Platform Assays for Efficient Development and When to Step Out of the Box**

*Sponsored by* FUJIFILM Diosynth biotechnologies

*Jason Barker, Ph.D., Associate Principal Scientist, Group Leader, Analytical Development, FUJIFILM Diosynth Biotechnologies*

Platform analytical methods are efficiently leveraged for efficient support monoclonal antibody and other recombinant protein throughout their development lifecycles. Method toolbox provides a stable baseline for development, yet stepping outside the method toolbox to develop methods for unique proteins or improve method robustness for long term use maybe required.

**12:15 pm Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

**1:00 Session Break**

## EMERGING MODALITIES

**1:45 Chairperson's Remarks**
*Lintao Wang, Ph.D., Principal Scientist and Mass Spec Group Leader, Analytical and Pharmaceutical Science, ImmunoGen, Inc.*

**1:50 Comparative Assessment of Physical and Chemical Stability of Bispecific Antibodies Using Different Analytical Tools**
*Prakash Manikwar, Ph.D., Scientist, MedImmune*

Mab-based bispecific antibodies (BiSAbs) offer a unique development challenges due to the presence of an additional single chain variable fragment (scFv) domain. We investigated physical and chemical stability of various BiSAb formats which differed in the location of scFv and antigen specificity using different analytical tools. Here, we compare the rate constants derived from different methods across the constructs and similarities between specificities along with analytical challenges and mechanistic understanding.

**2:20 Early Analytical Support for Novel Site-Specific ADC Development by Mass Spectrometry**
*Lintao Wang, Ph.D., Principal Scientist and Mass Spec Group Leader, Analytical and Pharmaceutical Science, ImmunoGen, Inc.*

ADCs continue to be a promising biotherapeutic approach for novel cancer therapies. A typical ADC is composed of several potent cytotoxic molecules covalently linked with a tumor-targeting monoclonal antibody in a site-specific or non-specific manner. SERIMAB technology has been recently explored to create site-specific novel DNA-alkylating IGN conjugates for preclinical evaluation. Mass spectrometry was efficiently used for early process

optimization, early-stage product characterization and *in vivo* stability assessment.

**2:50 Characterization of Novel General Amyloid Interaction Motif (GAIM)-Immunoglobulin (Ig) Fusions Targeting Misfolded Protein Aggregates in Neurodegenerative Diseases**

*Ming Proschitsky, Ph.D., Senior Scientist, Research, Proclara Biosciences*

Amyloids as therapeutic targets are heterogeneous and are well known to be difficult to analyze. Nevertheless, Proclara Biosciences developed specific SPR, ELISA and aggregation inhibition assays with high quality and consistency to characterize therapeutics interaction with amyloids. This presentation will illustrate how the challenges were addressed by adapting traditional analytical assays which otherwise only work well with soluble and homogeneous targets.

**3:20 Phase Appropriate Analytical Characterization of Recombinant Protein Based Vaccines**

*Vaneet K. Sharma, Ph.D., Analytical Scientist, Vaccine Development & Manufacturing, International AIDS Vaccine Initiative (IAVI)*

This presentation will outline key considerations towards the phase appropriate analytical characterization of recombinant protein based vaccines. Analytical strategies for the assay development, assay qualification and characterizing the critical quality attributes (CQAs) relevant to Phase I/II clinical trial material will be discussed. A case study will be presented to demonstrate the application of the phase appropriate characterization to support recombinant protein based vaccines development.

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

**4:45 PLENARY KEYNOTE PRESENTATION**

*(See page 3 for details.)*

**6:00 Networking Reception in the Exhibit Hall with Poster Viewing**

**7:00 Close of Day**

## THURSDAY, AUGUST 24

**8:00 am Registration Open and Morning Coffee**

## OPTIMIZING THE SPEED AND EFFICIENCY OF EARLY ANALYTICAL DEVELOPMENT

**8:25 Chairperson's Remarks**

*Marina Kirkitadze, Ph.D., Deputy Director, Head of Biophysics and Conformation Unit, Analytical R&D Biochemistry, Sanofi Pasteur, Canada*

**8:30 Insights from Native Mass Spectrometry and Ion Mobility-Mass Spectrometry for Antibody and Antibody-Based Product Characterization**

*Sarah Sanglier-Cianférani, Ph.D., Professor, University of Strasbourg, France*

Monoclonal antibodies-based products have emerged as one of the most successful classes of therapeutics. Mass spectrometric approaches play a central role in their analytical and structural multi-level characterization. Importantly, techniques allowing the characterization of intact mAb-based products under non-denaturing conditions are attracting increasing interest. Here, I will review the current state of the art in native mass spectrometry and ion mobility methods for the characterization of mAbs and mAb-based products.

**9:00 Integrating Novel Tools into Development Workflow of Biologics: NanoDSF and MST for Early Discovery and Developability Assessment**

*Alexey Rak, Ph.D., Head of Biostructure and Biophysics, Integrated Drug Discovery, Sanofi R&D, France*

Modern drug discovery operations require characterization of biomolecular interactions to be both time- and cost-effective as well as to be highly precise and reproducible. Here we report applications of two novel predictive, precise, low protein consuming and high throughput methods: nano-Differential Scanning Fluorimetry (nanoDSF) and MicroScale Thermophoresis (MST) applied in our biologics discovery and characterization operations. Examples of the demonstrated effectiveness of the nanoDSF and MST will be discussed.

**9:30 Featured Poster Presentation: Innovation of Cell Based Assay Platforms for Therapeutic mAb Against Viral Infection**

*Dengyun "Daisy" Sun, Ph.D., Senior Scientist, Biologics Analytical Science, Merck Research Laboratory*

There is increasing demand for mAb therapies to confer passive immunity against viral infection due to lack of vaccine or virus specific therapy. A functional cell based assay is a regulatory requirement for clinical development, commercial release and stability testing. This presentation discusses three novel cell based assay platforms in support of therapeutic mAb development against viral infection. The advantages and disadvantages of the platforms are compared.

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

**10:45 High Throughput Analytical Platforms for Early Biopharmaceutical Development**

*Vladimir Razinkov, Ph.D., Principal Scientist, Amgen*

The highly competitive landscape of the biopharmaceutical industry calls for a large number of candidates and an accelerated pipeline during early development. With constantly increasing complexity of new modalities and tight resources available at early development stage, the need for fast characterization screening of many candidates is in high demand. The presentation describes recent practices in the development and implementation of high throughput analytical methods during early candidate and formulation selection.

**11:15 Development and Adaptation of Platformed Analytical Approaches**

*Marina Kirkitadze, Ph.D., Deputy Director, Head of Biophysics and Conformation Unit, Analytical R&D Biochemistry, Sanofi Pasteur, Canada*

This presentation discusses the adaptation of platform methods to characterize higher order structure of protein antigens, enable insights in formulation stability, and support process development.

**11:45 Early Developability Evaluation of IgG-Based Novel Biologics Formats**

*Dana Filoti, Ph.D., Senior Scientist, Drug Product Development Preformulation, AbbVie*

Complex IgG-based novel biologics are remarkable from a biological MOA perspective and from a drug product developability profile. Linking drug discovery to upstream development of IgG-based novel formats

## THURSDAY, AUGUST 24

**11:30 am Registration Open**

**12:15 pm Enjoy Lunch on Your Own**

**1:15 Dessert Refreshment Break in the Exhibit Hall and Last Chance for Poster Viewing**

**1:55 Chairperson's Remarks**
*John F. Kellie, Ph.D., Associate Fellow, GlaxoSmithKline*

**2:00 KEYNOTE PRESENTATION: Process Control in an Era of Novel Biotherapeutics and New Technologies**
*Hao Chen, Ph.D., Director, Process Development & Engineering, Biologics & Vaccines, Merck & Co., Inc.*

As the biologics market and pipeline grew significantly in recent years, the industry entered an era of novel modalities and new technologies, which brings both challenges and opportunities for process control: 1) medical breakthroughs with mAbs and novel modalities demand expedited development; 2) continuous manufacturing is gaining momentum for efficiency and low cost; 3) new technologies including single use technology and systems biology bring improved process efficiency and understanding.

## DEVELOPING PROCESS UNDERSTANDING

**2:45 NIR Evaluation and Applications in Upstream Process Development and Manufacturing**
*Brian Kenty, Ph.D., Scientist, Manufacturing Sciences and Technology, MedImmune*

Monitoring nutrient and metabolite concentrations in a cell culture process is an essential aspect of the upstream biopharmaceutical manufacturing process. In this work, near infrared spectroscopy was used to establish quantitative online readings for multiple cell culture constituents in a fed-batch bioreactor process. Multivariate models were developed using data generated at bench-scale and were integrated with an automated process control system in a GMP manufacturing facility.

**3:15 MSApproaches for Monitoring Attributes: Connecting Forced Degradation Studies to Preclinical and Clinical Samples**
*John F. Kellie, Ph.D., Associate Fellow, GlaxoSmithKline*

CQAs are often identified through forced degradation studies and controlled through various manufacturing or formulation processes. Recent advances in MS technologies have enabled the quantification of CQAs from in-life study samples by MS-based assays. In-house approaches to achieve CQA monitoring from in-life samples will be discussed along with the advantages to such approaches, including identifying CQAs at an early stage and accelerated de-risking of CQAs.

**3:45 Featured Poster Presentation: Evaluating the Downstream Process Modifications of a Commercial Monoclonal Antibody**
*Zhi Li, Ph.D., Scientist, Bristol-Myers Squibb*

**4:00 Refreshment Break**

**4:15 Connecting Process to Product Quality – A Case Study**
*Swapnil Bhargava, Ph.D., Director, Bioprocess Development, Seattle Genetics*

Achieving and maintaining certain product quality attributes throughout the product lifecycle has been one of the main focus areas in recent years across the biotech industries. A thorough process-to-product quality understanding, which typically involved various aspects of process development groups, is essential to accomplish this goal. This study showcases an example of such collaboration among cell culture, analytical sciences and bioassay development groups to achieve targeted N-glycan profiles.

**4:45 Data Management in Process Development as a Key to Process Understanding and Development Efficiency**
*Martin Mayer, Ph.D., Director, evon GmbH, Austria*

Bioprocess development and characterization rely on reasonable DoEs, meaningful on- and offline process monitoring concepts and methods for automated data handling, analysis and interpretation including data integrity issues. An obstacle preventing the implementation of these key issues into bioprocess operation is the lack of GAMP5 conform process control software tools designed for fully automated management of complex bioprocess data sets. This talk introduces a software and workflow approach to tackle these problems.

**5:15 Close of Day**

**6:00 – 9:00 Recommended Dinner Short Courses***

**SC7: Analytical Strategies for Comparability in Bioprocess Development**

**SC9: Transient Protein Production in Mammalian Cells**

** Separate registration required, see page 6 for details.*

## FRIDAY, AUGUST 25

**8:00 am Registration Open and Morning Coffee**

## ONLINE AND INLINE PROCESS MONITORING

**8:25 Chairperson's Remarks**
*Udayanath Aich, Ph.D., Principal Scientist, Sanofi Genzyme*

**8:30 Improving Commercial Manufacturing Process Development through Inline and Online Technologies**
*Mandy Ly, Associate Scientist, Cell Culture Process Development, Amgen*

The development of commercial manufacturing processes is becoming increasingly complex as timelines shorten, therapeutic modalities diversify and cost reduction remains critical. To successfully meet these challenges, it is necessary to monitor and control critical process parameters in real-time or near real-time to meet necessary product quality attributes. Here we discuss various technologies and strategies to develop robust processes in this rapidly changing drug development landscape.

**9:00 Case Study: Enhancing Upstream Process Control, from Cell Expansion to Harvest**
*Brandon Moore, Engineer II, Cell Culture Development, Biogen*

This case study presents a PAT-centric approach to upstream process development which emphasizes the use of *in situ* biomass and other analytical probes for adaptive control during cell expansion and

antibody production. This control method allows us to de-risk error-prone inoculation operations and reduce reliance on process assumptions and historical knowledge when projecting process performance. The resulting process features improved early deviation detection and run-to-run consistency with more robust product quality profiles.

**9:30 Advances in Real Time and Near Real Time Measurement of Product and Process Related Attributes for Process Intermediates and End Product**

*Udayanath Aich, Ph.D., Principal Scientist, Biopharmaceutical Development, Sanofi-Genzyme*

The PAT and QbD regulatory initiatives have provided a foundation for shifting the paradigm away from end-process release testing to real-time release testing. This presentation will focus on the recent advances in on-line and at-line measurements of product and process attributes and describe the BioPhorum Operations Group's roadmap for ILM-RTR in industry practice and future vision for real-time release. We will also discuss case studies related to development and implementation of at-line measurement.

**10:00 Networking Coffee Break**

## CONTROL STRATEGIES

**10:30 Specification Development throughout the Product Lifecycle**

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

Product specifications evolve with the development stage of the program, with the test panel and acceptance criteria likely changing over time. This talk will focus on strategies to set initial product specifications for preclinical and Phase I, and how they evolve up to and post commercialization. Examples will include how the test panel is driven by CQAs and your overall control strategy.

**11:00 Setting Drug Substance CQA Acceptance Criteria and Incorporation into the Control Strategy and Specifications**

*Angela Lewandowski, Ph.D., Group Leader, Downstream Process Development, Bristol-Myers Squibb*

This talk will focus on the strategy employed for setting drug substance CQA acceptance criteria for incorporation into the in-process control strategy, and linkage of such criteria to the specifications. Case studies for both mAbs and Fc-fusion proteins will be discussed.

**11:30 A Playbook for Efficiently Creating and Maintaining a Holistic and Compliant Control Strategy for Legacy and New Products**

*Naveen Pathak, Director, Commercial CMC, Manufacturing Science & Technology, Shire Pharmaceuticals*

Creating and maintaining a holistic and compliant control strategy requires an efficient QbD methodology spanning all three stages of lifecycle PV, significant investment in product and process characterization data which is aligned with the methodology, and an IT infrastructure for risk management as well as automated acquisition and data analysis post commercialization. A playbook of how these factors come together to create such a control strategy will be discussed.

**12:00 pm Sponsored Presentation** *(Opportunity Available)*

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

**1:15 Session Break**

## OVERCOMING CHALLENGES IN PROCESS CHARACTERIZATION AND CONTROL

**1:25 Chairperson's Remarks**

*James Stonecypher, Ph.D., Senior Vice President, Head of Regulatory Affairs and Quality, Bonti*

**1:30 Current Trends in Biopharmaceuticals and Developing Fast Track Products**

*Frank J. Riske, Ph.D., Senior Consultant, BioProcess Technology Consultants, Inc.*

The biopharmaceutical landscape has changed dramatically in recent years. While early biologics were made in bacteria or yeast, mammalian cells are now the predominant. There has also been an explosion of gene and cell therapies and new technologies such as Crispr Cas9. We'll examine these trends and trends in developing molecules for orphan, fast-track, and breakthrough designations.

**2:00 Communicating Your Manufacturing Process in Regulatory Submissions: Leveraging the "Information Delta (Δ)"**

*James Stonecypher, Ph.D., Senior Vice President, Head of Regulatory Affairs and Quality, Bonti*

Significant thought and resources are put into process design, development, and control. The information that describes a manufacturing process in a regulatory submission often does not accurately reflect knowledge gains or current level of process-product understanding. This "information delta" contains valuable data that can be communicated in regulatory submissions to benefit developers. Opportunities for presenting manufacturing processes in regulatory submissions will be discussed.

**2:30 Leveraging Process Linkage and Challenge Studies to Define Control Strategies for Process Validation**

*Robert Vonder Reith, Senior Research Associate, Gilead Sciences*

Identification and control of critical process parameters and their proposed operating ranges are required to demonstrate a suitable control strategy. To accelerate the classification of these parameters, challenge linkage studies, starting from cell culture throughout the downstream steps, were performed to assess the manufacturing process capabilities under "worst case" conditions for pre-determined CQAs. A control strategy and acceptable range was proposed based on the linkage study results and individual unit operation capabilities.

**3:30 End of Conference**

Register Online!

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# Formulation & Stability

The weeklong Formulation & Stability stream brings together experts in analytical and formulation sciences to share practical insights and case studies on rapid methods for analytical screening and development, biotherapeutic formulation development, development of high concentration protein formulations, application of high-throughput/high resolution screening tools in early stage development and prediction and manipulation for protein stability, higher order structure and instabilities. The three conferences together will feature cutting edge approaches for understanding and managing protein formulation development, HOS, excipient issues, aggregation, high viscosity, and rapid analytical methods to predict and screen formulation stability and quality issues.

2017 FORMULATION & STABILITY TRACKS

**AUGUST 21-22**

AGENDA Rapid Methods to Assess Quality & Stability of Biologics

AGENDA Overcoming Formulation Challenges for Biopharmaceutical Development

**AUGUST 23-24**

AGENDA High-Concentration Protein Formulations

**AUGUST 24-25**

AGENDA TRAINING SEMINAR: Introduction to Biologics Formulation & Delivery

## MONDAY, AUGUST 21

**8:00 am Short Course Registration Open**

**9:00 – 11:30 Recommended Morning Short Courses***

**SC4: Accelerated Stability Testing of Biologics**

** Separate registration required, see page 6 for details.*

**11:30 Main Conference Registration Open**

## FORMULATION & ANALYTICAL STRATEGY FOR DEVELOPING COMPETITIVE BIOLOGICS PRODUCTS

**1:00 pm Chairperson's Opening Remarks**

*Christopher J. Roberts, Ph.D., Professor, Chemical & Biomolecular Engineering, University of Delaware*

**1:10 KEYNOTE PRESENTATION: Developing Competitive Biologics Products Necessitates Combining Formulation Design, Process Development, and Device Integration**

*Yatin Gokarn, Ph.D., Head, Global Pharmaceutical Development Biologics, Sanofi Genzyme*

There is a higher need for designing and developing competitive biologics drug products in today's competitive biotherapeutics marketplace when many new modalities and new product formats are making their way to market and many promising leads continue to fill the research and development pipelines. A competitive patient-centric product requires a holistic product development strategy that takes into consideration formulation design, process development, analytics and device integration.

**1:45 How Well Can We Predict Protein-Protein Interactions and Aggregation Propensity Using Molecular Models during Candidate and Formulation Assessment?**

*Christopher J. Roberts, Ph.D., Professor, Chemical & Biomolecular Engineering, University of Delaware*

The presentation will focus on approaches for identifying aggregation-prone proteins and formulation conditions based on different structural models and molecular simulation, compared to experimental results for protein-protein interactions and aggregation rates. Examples will include monoclonal antibodies and globular proteins at low and high concentrations, with a view to both candidate selection and formulation development.

**2:15 Divide and Conquer: Comparison of Statistical and Probabilistic Tools for Risk Assessment in Multi-Stage Processes**

*Olga Yee, Ph.D., Principal Scientist, Drug Product Science and Technology, Bristol-Myers Squibb*

Faster decisions imply acceptance of risks associated with accelerated development of compounds. In this presentation, a risk of success for a drug to meet a specification limit is quantified for a three-stage process using three approaches: worst-case scenario, variance transmission model, and the novel approach of "divide and conquer." A case study for a biologic drug product lifecycle from drug substance to final delivery is presented.

**2:45 Refreshment Break**

**3:15 Connecting Prescreening Studies to Commercial Product Stability and Integrity**

*Mark Brader, Ph.D., Research Fellow, Moderna Therapeutics*

Evaluating conformational and colloidal stability represents distinct aspects in the development of scalable bioproducts. An effective early development program will incorporate a diverse set of screening methodologies to evaluate drug candidates and their responses to solution conditions. Traditional and emerging approaches to the accelerated prediction of long term product stability will be reviewed and a perspective presented on leveraging biophysical methods to more effectively support comparability and biosimilarity assessments.

**3:45 High Throughput, Low Volume Subvisible Particle Screening**

*Sponsored by* halo labs

*Bernardo Cordovez, Ph.D., President, Halo Labs*

Halo labs will present a subvisible particle screening tool, the HORIZON, with detailed explanation of its Backgrounded Membrane Imaging (BMI) technology. A comparative analysis between HORIZON and flow imaging will be presented and key performance indicators including sample volume, throughput, dynamic range, instrument repeatability will be evaluated.

**4:00 Approaches to Extractables/ Leachables for Single Use Systems: Case Studies Using a Risk-based Approach**

*Sponsored by* U.S. Manufacturing and Testing | Biologics • Advanced Therapies • Medical Devices

*Sandi Schaible, Director, Analytical Chemistry, WuXi AppTec*

There are a number of approaches when it comes to Extractables/Leachables testing for Single Use Systems in bio manufacturing. We will discuss taking a customized approach based on the risk of each component in your system.

**4:30 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.

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

**7:00 End of Day**

# Rapid Methods to Assess Quality & Stability of Biologics:

Improving Prediction and Screening

## TUESDAY, AUGUST 22

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

## RAPID METHODS FOR STABILITY AND PRODUCT QUALITY SCREENING

**7:55 Chairperson's Remarks**

*Czeslaw Radziejewski, Ph.D., Senior Principal Research Scientist, Biophysical Chemistry, AbbVie*

**8:00 High Throughput Sialic Acid Analysis**

*Yimin Hua, Ph.D., Scientist II, Global Manufacturing Science and Technology - Analytical Science and Technology, Sanofi*

The level of sialic acid is a critical quality attribute for therapeutic proteins. The level of sialic acid can be measured through glycan profiling which typically involves lengthy sample preparation procedure and challenges in separation of various glycans. This presentation will talk about a high throughput method with simple procedure for the determination of sialic acid level in glycoproteins. This method is not only QC user friendly, but also can be used for fast screening in product and process development.

**8:30 Rapid Minor Variants Identification in Therapeutic Antibodies by an Automatic Off-Line 2D-LC/Q Exactive® System**

*Jin Li, Ph.D., Senior Research Associate, Analytical Development and Quality Control, Genentech, Inc.*

Understanding the chemical nature of minor variants in therapeutic proteins is critical for process development and product quality control. The current techniques for minor variant characterization typically require manual fractionation to enrich the low abundance species followed by desalting procedures to make the sample MS compatible. Herein we developed a rapid and automatic off-line 2D-LC/Q Exactive® MS workflow for mass analysis of the minor variants in a therapeutic antibody.

**9:00 High-Throughput Analytics from RoboColumn Purification to Product Quality Screening**

*Hardip Gopani, Development Associate III, Analytical & Pharmaceutical Sciences, ImmunoGen, Inc.*

With the increased use of automation in cell line screening and small scale upstream process development, demand for high-throughput analytics continues to grow. The right assay platforms and strategic choice of product quality to screen enabled us to meet these needs. We will share our experience with setting up an automated RoboColumn purification platform for the testing of antibody harvest cell culture fluid (HCCF) samples.

**9:30 High-Throughput Light Scattering Tools for Characterizing and Formulating Macromolecules and Nanoparticles**

*Sponsored by* WYATT TECHNOLOGY

*Julia Deuel, Applications Scientist, Wyatt Technology*

From aggregates to conjugates, peptides to polysaccharides, light scattering detectors provide a comprehensive suite of biophysical characterization tools. The light scattering toolkit determines molar mass, size, charge, interactions, and conjugation of macromolecules and nanoparticles. This seminar presents an overview of the instrumentation and example applications, focusing on µSEC-MALS-DLS, and HT-DLS.

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

**10:30 Novel Approach towards the Evaluation of Critical Quality Attributes and Stability of Proteins**

*Belinda Pastrana, Ph.D., Full Professor, Department of Chemistry, University of Puerto Rico, Mayaguez Campus*

Therapeutic proteins are highly complex molecules; their CQAs require diverse bioanalytical techniques to comply with reporting requirements to regulatory agencies. Ideally a multivariate analysis would also be needed to address stability, yet even under the current state of technology, including proteomic and high resolution, techniques can be costly and time consuming. We have developed a DOE, label free method using Best-in-Class platform technology to aid in addressing this concern.

**11:00 Rapid Method for Total Protein Measurement Using SoloVPE Technology – Challenges and Solutions**

*Hsin-I Peng, Ph.D., Associate Manager, Quality Control, Regeneron Pharmaceuticals, Inc.*

SoloVPE technology presents a unique platform for protein concentration measurement with key benefits including "no dilution" and "rapid reading." When exploiting SoloVPE, protein concentration under-estimation is experienced for highly concentrated samples, posing challenges for accurate protein concentration measurement. Our studies show standard curve data collected outside the Beer's law linear region can unfavorably result in protein under-estimation. Challenges and solutions when using SoloVPE technology for protein measurement will be ...

**11:30 pm Punch up Biologic Development with ΔG and the HUNK**

*Sponsored by* UNCHAINED LABS

*Greg Manley, Ph.D., Senior Applications Scientist, Unchained Labs*

Developing biologics requires identifying an ideal construct followed by assessing a wide range of formulation space to ensure stability and minimize aggregate. Assessing ΔG is a powerful approach for the quantitative assessment of conformational stability and aggregation. The HUNK automates the tedious and manual task of determining ΔG, allowing for quantitative stability assessment throughout biologic development. We'll discuss how HUNK can be used in conjunction with more traditional approaches to assessing stability and aggregation propensity.

**12:00 High Throughput Methods to Assess Stability of Biologics During Pre-Formulation and Formulation Development**

*Smita Raghava, Ph.D., Senior Scientist, Sterile Formulation Sciences, Merck*

There is a growing demand in the pharmaceutical industry for developing orthogonal tools to accurately, rapidly, and reproducibly predict protein solution stability behaviors using limited material to improve formulation screening and manufacturability assessment. This presentation will focus on combination of high-throughput technologies and assays for formulation and drug product development of biologics, such as monoclonal antibodies (mAbs)

and mAb-based modalities. The overview of tools, their novel implementation, and relationship to commonly conducted "stability studies" will be further discussed using examples of high-throughput workflows, pre-formulation screening, and formulation development/optimization.

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

1:15 **Dessert Refreshment Break in the Exhibit Hall with Poster Viewing**

## HIGHER ORDER STRUCTURE, COMPARABILITY, PARTICLES AND STABILITY

1:55 **Chairperson's Remarks**
*Haripada Maity, Ph.D., Research Advisor, Formulation Development, CMC Development, Eli Lilly and Company*

2:00 **Critical Considerations in the Characterization of Protein Higher Order Structure (HOS) and Its Relationship with Stability and Function**
*Haripada Maity, Ph.D., Research Advisor, Formulation Development, CMC Development, Eli Lilly and Company*
Higher order structure (HOS) of a protein can be altered due to both physical and chemical instabilities. Characterization of HOS is important in assessing comparability, formulation and process development. This presentation will discuss the (i) selection of techniques in characterization of HOS, (ii) quantitative and qualitative evaluation of characterization parameters and their sensitivity and precision, and (iii) the effect of chemical "mutagenesis" on HOS, stability and functional properties.

2:30 **Selected Poster Presentation: Challenges in Characterization Of Bioprocesses and Products using Raman spectroscopy**
*Dimuthu Jayawickrama, Ph.D., Sr. Research Investigator II, Drug Science Product & Technology, Bristol-Myers Squibb Company*
Raman spectroscopy is a viable spectroscopic tool to analyze biological samples. Raman's spectral specificity for molecules, insensitivity to water and ability to analyze without sample manipulation are attractive features. In this presentation challenges for two different real-time Raman applications. In one example the effect of fluorescence background, cells/debris, and spectral interference on spectra during in-situ cell culture monitoring is discussed. In another example challenges for characterization of intact protein solutions are presented.

3:00 **Selected Poster Presentation: Higher Order Structural View of The Effects of Oxidation on The Structure, Stability and Aggregation of Interferon Alpha-2a**
*Dinen Shah, Ph.D Candidate, Pharmaceutical Sciences, University of Colorado Denver*
Oxidation of therapeutic proteins during their formulation and shelf-life is a persistent challenge facing the biopharma industry. We used IFN-alpha 2a to obtain a mechanistic understanding of how oxidation affects its structure, stability, aggregation and function. Using high resolution techniques such as 2D NMR helped us to pinpoint the residue level structural changes that correlate with functional changes.

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

4:15 **Using Endoglycosidase and High Resolution Mass Spectrometry to Estimate the Level of MAN-5 and Afucosylation in Monoclonal Antibodies**
*Ming-Ching Hsieh, Ph.D., Research Advisor, BioAnalytical Science, Eli Lilly and Company*
This presentation will discuss a rapid glycosylation analysis using fast fluorescent labeling for overall glycan profiles and endoglycosidases with site specific protease for estimation of MAN-5 glycan and afucosylation levels in biologics.

4:45 **Understanding & Verifying Flow Imaging Particle Counters**
*Dean Ripple, Ph.D., Leader, Bioprocess Measurements Group, National Institute of Standards and Technology*
Flow imaging instruments can measure particles in biotherapeutics with potentially greater accuracy than light obscuration. However, verification methods for flow imaging instruments are not yet standardized. I will present methods used to verify the performance of flow imaging particle counters. Topics will include the use of reference materials, examination of data self-consistency, and solutions to common problems. Methods to understand errors in counts and reported size will also be presented.

5:15 **Close of Conference**

6:00 – 8:30 **Recommended Dinner Short Course***
**SC8: Protein Aggregation: Mechanism, Characterization and Consequences**
** Separate registration required, see page 6 for details.*

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# 5TH ANNUAL Overcoming Formulation Challenges for Biopharmaceutical Development:

Formulation and Process Optimization, Excipients, Analytics and Device Integration

## MONDAY, AUGUST 21

**8:00 am Short Course Registration Open**

**9:00 – 11:30 Recommended Morning Short Courses***

**SC4: Accelerated Stability Testing of Biologics**

** Separate registration required, see page 6 for details.*

**11:30 Main Conference Registration Open**

## FORMULATION & ANALYTICAL STRATEGY FOR DEVELOPING COMPETITIVE BIOLOGICS PRODUCTS

**1:00 pm Chairperson's Opening Remarks**

*Christopher J. Roberts, Ph.D., Professor, Chemical & Biomolecular Engineering, University of Delaware*

**1:10 KEYNOTE PRESENTATION: Developing Competitive Biologics Products Necessitates Combining Formulation Design, Process Development, and Device Integration**

*Yatin Gokarn, Ph.D., Head, Global Pharmaceutical Development Biologics, Sanofi Genzyme*

There is a higher need for designing and developing competitive biologics drug products in today's competitive biotherapeutics marketplace when many new modalities and new product formats are making their way to market and many promising leads continue to fill the research and development pipelines. A competitive patient-centric product requires a holistic product development strategy that takes into consideration formulation design, process development, analytics and device integration.

**1:45 How Well Can We Predict Protein-Protein Interactions and Aggregation Propensity Using Molecular Models during Candidate and Formulation Assessment?**

*Christopher J. Roberts, Ph.D., Professor, Chemical & Biomolecular Engineering, University of Delaware*

The presentation will focus on approaches for identifying aggregation-prone proteins and formulation conditions based on different structural models and molecular simulation, compared to experimental results for protein-protein interactions and aggregation rates. Examples will include monoclonal antibodies and globular proteins at low and high concentrations, with a view to both candidate selection and formulation development.

**2:15 Divide and Conquer: Comparison of Statistical and Probabilistic Tools for Risk Assessment in Multi-Stage Processes**

*Olga Yee, Ph.D., Principal Scientist, Drug Product Science and Technology, Bristol-Myers Squibb*

Faster decisions imply acceptance of risks associated with accelerated development of compounds. In this presentation, a risk of success for a drug to meet a specification limit is quantified for a three-stage process using three approaches: worst-case scenario, variance transmission model, and the novel approach of "divide and conquer." A case study for a biologic drug product lifecycle from drug substance to final delivery is presented.

**2:45 Refreshment Break**

**3:15 Connecting Prescreening Studies to Commercial Product Stability and Integrity**

*Mark Brader, Ph.D., Research Fellow, Moderna Therapeutics*

Evaluating conformational and colloidal stability represents distinct aspects in the development of scalable bioproducts. An effective early development program will incorporate a diverse set of screening methodologies to evaluate drug candidates and their responses to solution conditions. Traditional and emerging approaches to the accelerated prediction of long term product stability will be reviewed and a perspective presented on leveraging biophysical methods to more effectively support comparability and biosimilarity assessments.

**3:45 High Throughput, Low Volume Subvisible Particle Screening**

*Sponsored by* halo labs

*Bernardo Cordovez, Ph.D., President, Halo Labs*

Halo labs will present a subvisible particle screening tool, the HORIZON, with detailed explanation of its Backgrounded Membrane Imaging (BMI) technology. A comparative analysis between HORIZON and flow imaging will be presented and key performance indicators including sample volume, throughput, dynamic range, instrument repeatability will be evaluated.

**4:00 Approaches to Extractables/Leachables for Single Use Systems: Case Studies Using a Risk-based Approach**

*Sponsored by* U.S. Manufacturing and Testing | Biologics • Advanced Therapies • Medical Devices

*Sandi Schaible, Director, Analytical Chemistry, WuXi AppTec*

There are a number of approaches when it comes to Extractables/Leachables testing for Single Use Systems in bio manufacturing. We will discuss taking a customized approach based on the risk of each component in your system.

**4:30 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.

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

**7:00 Close of Day**

## TUESDAY, AUGUST 22

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

## EXCIPIENTS & SURFACTANT STABILITY IN BIOPHARMACEUTICAL FORMULATIONS

**7:55 Chairperson's Remarks**

*Andrea Hawe, Ph.D., CSO, Coriolis Pharma*

# 5TH ANNUAL Overcoming Formulation Challenges for Biopharmaceutical Development:

Formulation and Process Optimization, Excipients, Analytics and Device Integration



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**8:00 Trends on Analytical Characterization of Polysorbates and Their Degradation Products in Biopharmaceutical Formulations**

*Andrea Hawe, Ph.D., CSO, Coriolis Pharma*

Polysorbate 20 and 80 are the most common surfactants in biopharmaceutical products. Structural heterogeneity, presence of degradants, impurities, and tendency for degradation may impact their functional properties and pose a challenge for the analytical characterization of PS at different stages of product development. The talk focuses on methods and strategies for the analytical characterization of PS, their degradants and other impurities within neat PS and in biopharmaceutical formulations.

**8:30 Understanding the Impact of Histidine and Polysorbate 20 Degradation in Stainless Steel Containers on Protein Aggregation and Stability**

*Adithi Chandrasekhara, Research Associate, Late Stage Pharmaceutical Development, Genentech, Inc.*

Histidine and polysorbate 20, commonly used in biologics formulations, degrade substantially when stored in stainless steel containers at accelerated temperatures (≥25°C). The observed degradation is catalyzed by metal ions leaching from the containers and is synergistic and rapid when both histidine and PS20 are present. The impact of these degraded excipients on protein aggregation and stability was characterized to assess the risk of accelerated temperature exposure to stainless steel containers.

**9:00 Polysorbate Interactions with Monoclonal Antibodies as Probed by 2D NMR**

*Krishna M.G. Mallela, Ph.D., Associate Professor of Biophysical Chemistry, Department of Pharmaceutical Sciences, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus*

We examined how polysorbates affect the structure of a monoclonal antibody using 2D NMR. Both bind to the antibody with a millimolar affinity. Binding induced changes in the tertiary structure with no changes in the secondary structure. The Fab region showed significant changes in the NMR spectrum compared to no changes in the Fc region, which indicates that polysorbates preferentially interact with the Fab region rather than the Fc region.

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

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

## CHALLENGES OF LOW & HIGH CONCENTRATION FORMULATIONS

**10:30 Intravenous Administration of Low Concentration Formulations**

*Ian Lent, MS, Development Associate II, MacroGenics, Inc.*

Dart® molecules are bi-specific antibody-based proteins developed for various indications including immune-oncology. These molecules are manufactured using conventional antibody platforms, and demonstrate product quality and stability comparable to conventional antibodies. The increased potency and lower concentration formulations of certain bi-specific molecules present new challenges for intravenous administration. Case studies will be presented regarding approaches for IV administration of low concentration protein formulations that highlight diluent, administration and analytical challenges.11:00 Transformational Science: Moving from Challenges of High Concentration Protein Formulations Development to Meet the Needs of Highly Potent Bispecifics

*Sachin Dubey, Ph.D., Head of Formulation Development, Process Development, Glenmark Pharmaceuticals SA*

**11:00 Transformational Science: Moving from Challenges of High Concentration Protein Formulations Development to Meet the Needs of Highly Potent Bispecifics**

*Sachin Dubey, Ph.D., Head of Formulation Development, Process Development, Glenmark Pharmaceuticals SA*

**11:30 Designing a Low Viscosity, High Concentration Protein Formulation**

*Sarah Altinoglu, Ph.D., Post-Doctoral Scientist, Bioproduct Research and Development, Eli Lilly and Company*

Although a universal formulation strategy to decrease viscosity of protein drugs is unrealistic, a better understanding of the connection between molecular properties and viscosity can help to reduce the complexity and time commitment involved in high concentration protein formulation. Here, we have studied this connection and analyzed how these findings can guide future protein formulations.

**12:00 pm An Assessment of Self Interaction Chromatography as a Rapid Tool to Investigate Protein-Protein Interactions and Its Application in Formulation Screening Workflows**

*Sanket Patke, Ph.D., Research Investigator, Drug Product Science and Technology, Pharmaceutical Development, Bristol-Myers Squibb*

Protein-protein interactions influence colloidal stability parameters such as solubility and aggregation. Measurement of osmotic second-virial coefficients, B22, provides one method to quantify protein interactions at the molecular level. Self-interaction chromatography is a novel method of measuring B22 with modest material and time requirements. Here we discuss the application of this approach to investigate protein–protein interactions in mAbs. This approach can potentially be used as a tool during formulation screening.

**12:30 Luncheon Presentation: Up Your Game in Protein Quantitation - Higher Throughput and Concentrations**

*Sponsored by* UNCHAINED LABS

*Tony Montoye, Director, Product Marketing, Unchained Labs*

See how Unchained Labs brings micro-volume DNA/RNA and protein quantification to the next level by eliminating all manual prep, dilutions or risk of cross-contamination. All you need is 2 µL and 5 minutes to measure up to 96 samples, even at high concentrations. Get biologics and genomics UV/Vis quantification on the money every time.

**1:15 Dessert Refreshment Break in the Exhibit Hall with Poster Viewing**

## LYOPHILIZATION OF NEW MODALITIES & PROCESS OPTIMIZATION

**1:55 Chairperson's Remarks**
*Haresh T. More, Ph.D., Research Investigator I, Parenteral Science and Technology, Bristol-Myers Squibb*

**2:00 Lyophilization of Antibody-Drug Conjugates (ADCs) Containing Highly Potent Cytotoxic Agents**
*Amit Gangar, Ph.D., Scientist I, Drug Product and Process Development, Immunogen, Inc.*
Handling and stabilizing cytotoxic ADCs poses several challenges to formulation development scientists. While developing a lyophilized formulation is the most common approach, additional formulation and safety concerns need to be evaluated. This presentation will provide insight into developing robust lyophilized ADC formulations while minimizing risk of exposure to the developers.

**2:20 Investigation of Fogging/Haze Behavior in Lyophilized Drug Product**
*Min Huang, Ph.D., Principal Scientist, Pharmaceutical Research and Development, Pfizer, Inc.*
Experiments were performed in this study to understand the fogging phenomena in the lyophilized drug product vials. This study demonstrated that many parameters including glass vial surface, vial treatment, lyophilization process, protein concentration and drug product formulation all could potentially affect the vial fogging phenomena to some extent. In addition, the study looked into the potential impact of fogging behavior in lyophilized drug product vials to the container closure integrity.

**2:40 Lyophilization Process Optimization and Identification of Design Space for Monoclonal Antibody Formulation Using Definitive Screening Design**
*Haresh T. More, Ph.D., Research Investigator I, Parenteral Science and Technology, Bristol-Myers Squibb*
The lyophilization process optimization for any new drug formulation requires multiple runs to identify the optimal shelf temperature, chamber pressure, and primary drying time. In this study, a definitive screening DOE was used to evaluate and identify product and process design space in an integrated fashion, where the effects of eight formulation and process factors were explored with a minimal number of lyophilization experiments.

**3:10 Spray-Freezing and Dynamic Bulk Freeze Drying: An Innovative Technology for Production of a Stable, Free-Flowing Bulk Powder from a High-Volume Liquid mAb Product**
*Deirdre Lowe, Senior Engineer I, Technical Development, Biogen*
The inherent instability of protein therapeutics at room temperature often requires a cold supply chain for storage, shipping and handling. For high-volume products, cold supply chain logistics are particularly challenging and expensive. In the case study presented here, a semi-continuous process is described for converting a high-volume liquid mAb product into a free-flowing bulk powder that is stable at room temperature. This technology has many advantages compared to conventional spray-drying and freeze-drying methods that further enable multiple drug product development options. Equipment, formulation and processing considerations for implementing this technology will be discussed in detail.

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

## PROCESSES, PLATFORM APPROACHES & PRODUCT QUALITY

**4:15 Degradation of mAbs during Manufacturing and Filling: An Underlying Mechanism and Common Origin of the Problem Explored**
*Tatiana Nanda, Ph.D., Biopharm Product Development Investigator, Biopharm Product Sciences, GlaxoSmithKline*
Exposure to various interfaces during production, shipment and storage may be a contributing factor in degradation of protein therapeutics. Currently there is no consensus view on whether surface interaction or shear stress, or a combination of these are causative for protein aggregation. We subjected several mAbs to shear stress/surface interactions resembling manufacturing and injection conditions. The consistency in aggregate types formed in the systems advocates for a common degradation pathway.

**4:45 Challenges in Handling of the Platform Formulations from Development through Marketing Application**
*Radhakrishna Maroju, Ph.D., Senior Scientist, Biologics CMC, Teva Biopharmaceuticals USA*
A growing trend in the industry is to use platform formulations for Phase I products and carry it over through commercialization when feasible. The talk will present the common challenges that may be encountered in use of a platform formulation especially in late phase development to support a marketing application. Use of some novel multidimensional diagrams to identify suitability of a Phase I formulation to be carried over early in late phase will be demonstrated.

**5:15 Close of Conference**

**6:00 – 8:30 Recommended Dinner Short Course***
**SC8: Protein Aggregation: Mechanism, Characterization and Consequences**
** Separate registration required, see page 6 for details.*

## WEDNESDAY, AUGUST 23

**7:00 am Registration Open and Morning Coffee**

## PROTEIN-PROTEIN INTERACTIONS, AGGREGATION & FORMULATION DEVELOPMENT

**8:05 Chairperson's Opening Remarks**

*Tom Laue, Ph.D., Professor Emeritus, Biochemistry, University of New Hampshire*

**8:15 KEYNOTE PRESENTATION: Considerations of Protein Solubility for High Concentration Formulation Development**

*Jifeng Zhang, Ph.D., Senior Director, Global Head of Device-ability, Global Pharmaceutical Development Biologics, Pharmaceutical Development Biologics, Sanofi*

Low protein solubility and high viscosity of solution are some of the major challenges in development, manufacturing and delivery of high concentration protein formulation. In this presentation, we will discuss various considerations and strategies to overcome the protein solubility issue for high concentration protein formulation development.

**9:00 Probing Complex Protein-Protein Interactions at High Concentrations**

*Tom Laue, Ph.D., Professor Emeritus, Biochemistry, University of New Hampshire*

There are several methods for detecting and characterizing high-concentration, protein-protein interactions when there is only one protein component. However, high-concentration formulations may contain several components and species. Furthermore, high-concentration formulations will be introduced into complex, concentrated solutions, such as serum. Fluorescence-detected analytical ultracentrifugation (AU-FDS) provides a first-principle method for characterizing the behavior of a single component in a complex mixture. Insights provided by AU-FDS for both single-component formulations and serum will be presented and discussed.

**9:30 Predicting High-Concentration Behavior from Low-Concentration Data: Need for Caution**

*Atul Saluja, Ph.D., Associate Director, Global Pharmaceutical Development Biologics, Sanofi*

Prediction of aggregation behavior (rates or trends per se) many times becomes necessary either as a function of temperature or protein concentration. Such approaches routinely rely on linear analysis wherein trends at lower protein concentration are projected to hold at higher protein concentrations. In this talk, data will be presented to emphasize the need for caution in employing such a linear predictive approach. Potential pitfalls in predicting optimal formulation conditions for concentrated solutions from dilute solution data will also be highlighted.

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

*Sponsored by* ROCKLAND antibodies & assays

**10:45 Innovative Approaches to Achieving Stable High-Concentration Protein Compositions**

*Jan Jezek, Ph.D., CSO, Research & Development, Arecor, Ltd.*

The need to develop stable, low-viscosity formulations of therapeutic proteins is greater than ever, and new approaches to formulation are needed to overcome associated stability and viscosity challenges. The talk will describe several novel compositions of concentrated proteins allowing development of liquid high-concentration protein products with superior stability profiles, with a focus on the control of aggregation as well as other quality attributes such as viscosity and fragmentation.

**11:15 PANEL DISCUSSION: Opportunities and Challenges in Adoption and Implementation of Disruptive Technologies for High-Concentration Protein Formulations**

*Moderator:*

*Tom Laue, Ph.D., Professor Emeritus, Biochemistry, University of New Hampshire*

*Panelists:*

*Atul Saluja, Ph.D., Associate Director, Global Pharmaceutical Development Biologics, Sanofi*

*Jan Jezek, Ph.D., CSO, Research & Development, Arecor, Ltd.*

*Jifeng Zhang, Ph.D., Senior Director, Global Head of Device-ability, Global Pharmaceutical Development Biologics, Sanofi*

*Michael S. Marlow, Ph.D., Senior Staff Scientist, Protein Biochemistry, Regeneron Pharmaceuticals, Inc.*

**11:45 Particle Engineering Platform for High-Concentration Protein Suspensions**

*Sponsored by* Lindy Biosciences

*Deborah Bitterfield, Ph.D., CEO and Founder, Lindy Biosciences, LLC*

Suspension formulations can alleviate the viscosity and stability challenges associated with subcutaneous delivery of biologics. We will present a novel dehydration technology, Microglassification, which combines the stability of solid formulations with particle-engineering expertise. The resulting dense protein particles are ideal for high-concentration, injectable suspensions.

**12:15 pm Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

*1:00 Session Break*

## PROCESS AND MANUFACTURING CONSIDERATIONS FOR HIGH CONCENTRATION FORMULATIONS

**1:45 Chairperson's Remarks**

*Jan Jezek, Ph.D., CSO, Research & Development, Arecor, Ltd.*

**1:50 FEATURED PRESENTATION: Mechanistic Investigation on Grinding-Induced Subvisible Particle Formation during Mixing and Filling of Monoclonal Antibody Formulations**

*Yuh-Fun Maa, Ph.D., Senior Principal Engineer, Pharmaceutical Processing & Technology Development, Genentech, Inc. - A Member of the Roche Group*

Monoclonal antibody (mAb) particle formation observed during bottom mounted mixing and filling by piston pump was investigated to understand the root-cause mechanisms leading to subvisible particle formation. The design of the mixer and the pump plays a critical role and any designs with contacting moving parts may grind the mAb molecules to immediately form subvisible particles. Stress types

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associated with grinding action have been assessed in various stress models.

**2:20 Formulation and Process Strategies to Improve TFF Performance**

*Steven Geng, Ph.D., Research Scientist, Bioproduct Pharma Design, Eli Lilly and Company*

Desire for higher doses of biologics has driven a need to formulate at higher concentrations. Tangential flow filtration (TFF) is a commonly used unit operation to concentrate protein. Here we have identified and studied how to overcome factors that limit TFF performance.

**2:50 Upstream/Downstream Processing Impact on High-Concentration Formulation Stability: A Case Study**

*Steve Lantz, Scientist I, Protein Pharmaceutical Development, Biogen*

Changes to cell culture and purification processes impacted the aggregation stability of a high-concentration mAb formulation. This case study details the process controls established to maintain product quality and how formulation optimization inhibited aggregation related to certain chemical modifications.

**3:20 Use of First-Principles to Guide Process Development for High Concentration Protein Drug Product**

*Zhao Yu, Ph.D., Associate Senior Consultant Engineer, Bioproduct Research and Development, Eli Lilly and Company*

High concentration protein drug products often have higher viscosity and density, which may result in challenges in process development and manufacturing. This talk presents a case study where engineering principles and computational fluid dynamics modeling were used to achieve mechanistic understanding of the controlling parameters in a mixing operation. They also guided the design of experiments using surrogate fluids or drug product, which gave further validation of the process knowledge and provided scale-up rationale.

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

**4:45 PLENARY KEYNOTE PRESENTATION**

*(See page 3 for details.)*

**6:00 Networking Reception in the Exhibit Hall with Poster Viewing**

**7:00 Close of Day**

## THURSDAY, AUGUST 24

**8:00 am Registration Open and Morning Coffee**

## RAPID EXCIPIENT SCREENING

**8:25 Chairperson's Remarks**

*Atul Saluja, Ph.D., Associate Director, Global Pharmaceutical Development Biologics, Sanofi*

**8:30 Screening Formulation Conditions with High Concentration Self-Interaction Nanoparticle Spectroscopy (HC-SINS)**

*Michael S. Marlow, Ph.D., Senior Staff Scientist, Protein Biochemistry, Regeneron Pharmaceuticals, Inc.*

Manufacturing and dosing of therapeutic monoclonal antibodies frequently call for high protein concentration solutions and the non-ideality that follows complicates reliable extrapolation of critical properties from measurements made under dilute conditions. This talk will illustrate the utility of a novel implementation of SINS in bridging the dilute-high concentration gap by assessing the concentration dependence of protein-protein interactions and the effect various formulation strategies have on colloidal behavior.

**9:00 Preferential Interactions of Formulation Excipients with High-Concentration IgG1 Monoclonal Antibody Solutions**

*Chaitanya Sudrik, Postdoctoral Associate, Chemical Engineering, Massachusetts Institute of Technology*

The aggregation and viscosity behavior of high concentration mAb formulations is impacted by the addition of weakly interacting excipients. Here, we present the data for the preferential interaction of commonly used excipients like trehalose, L-arginine HCl and sodium chloride with three therapeutically relevant IgG1 antibody molecules. We also present data for the impact of excipient addition on protein stability and derive further insight on the underlying molecular mechanisms.

**9:30 Selected Poster Presentation: A Modeling Approach For Excipient Selection in High-Concentration Protein Formulations**

*Christoph Brandenbusch, Ph.D., Group Leader, Lab of Thermodynamics, Biochemical & Chemical Engineering, Technical Univ. of Dortmund*

HCPFs are commonly achieved by addition of suitable FDA approved excipients (e.g. salts, sugars, amino acids, surfactants) to aqueous protein solution based on heuristic approaches/decisions. This approach does not account for negative influences induced by the excipients (e.g. agglomeration) in early stage development. In this work, we present first results on a novel method to identify suitable excipients/ excipient combinations based on their intermolecular interactions with the protein in solution.

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

**10:45 Pre-Formulation Approaches to Understand Instabilities in Protein Solution**

*Ashlesha S. Raut, Ph.D., Senior Scientist, Biologics and Vaccine Formulation, Merck*

The aim of formulation development of protein therapeutics is to produce efficacious products wherein the protein remains in the solution and maintains stability across its shelf life. With the ever-growing biologics pipeline, continual efforts are directed towards the implementation of high throughput approaches to select robust candidate and formulation. This presentation discusses the impact of formulation and key process parameters on the protein stabilities and formulation selection strategies in the early stages of development.

## VISCOSITY, INJECTABILITY AND DELIVERY

**11:15 High Concentration Relative to What? Some Case Studies**

*Zahra Shahrokh, Ph.D., CMC Consultant and Chief Development Officer, STC Biologics*

For each protein, a high concentration is a relative term, where even 10 mg/ml might be a challenge, for example for a non-Mab entity, and achieving 10x higher concentration requires scientific and empirical development approaches. Meeting the toxicology delivery requirements of protein therapeutics can sometimes be a higher hurdle than the clinical

program in terms of product concentration and compositions. This talk with provide case examples of different types of proteins and delivery routes that necessitated creative approaches to formulation design.

**11:45 Challenges of High Protein Concentration Formulations for Ocular Drug Delivery**

*Meike Irngartinger, Ph.D., Senior Scientist, Early Stage Pharmaceutical and Process Development, F. Hoffmann-La Roche Ltd.*

Formulation development for ocular drug delivery is a highly challenging area when it must deal with high concentrations aiming on less frequent dosing schemes. Results of a case study on high concentration formulation development for ocular application will be presented. Further on, the challenge of high concentration combined with low fill volume on drug product manufacturing and administration is discussed.

**12:15 pm Enjoy Lunch on Your Own**

**1:15 Dessert Refreshment Break in the Exhibit Hall and Last Chance for Poster Viewing**

**1:55 Close of Conference**

# Cell Therapy

The weeklong Cell Therapy stream comprises two back-to-back conference tracks focusing on cell therapy regulation, CMC strategies, analysis, quality control, process development, technology development, scale-up and commercial manufacture of cell and gene-based products, with particular focus on CART and TCR therapies.
First stop is Cell Therapy CMC, Quality and Analytics which looks at latest regulations in US and EU followed by in depth sessions on potency assay development, flow cytometry, raw materials, release testing, target product profiles and quality control, followed by two days on Cell Therapy Manufacturing, taking in key topics such as cell therapy manufacturing, commercialization, scale-up, automation, closed systems, technology development, managing external partners and vein-to-vein supply.

2017 CELL THERAPY TRACKS

**AUGUST 21-22**

AGENDA Cell Therapy CMC, Quality & Analytics

**AUGUST 23-24**

AGENDA Cell Therapy Manufacturing, Operations & Logistics

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2ND ANNUAL

# Cell Therapy CMC, Quality and Analytics

## MONDAY, AUGUST 21

**8:00 am Short Course Registration Open**

**9:00 – 11:30 Recommended Morning Short Courses***

**SC2: Comparability Strategies for Cell and Gene Therapies**

** Separate registration required, see page 6 for details.*

**11:30 Main Conference Registration Open**

## CHALLENGES AND OPPORTUNITIES IN CELL THERAPY CMC

**1:00 pm Chairperson's Opening Remarks**

*Bernadette Keane, Ph.D., Consultant, Keane Consultancy*

**1:10 KEYNOTE PRESENTATION:**

**Challenges and Opportunities in Cell Therapy CMC: The Role of CQAs, In-Line Measurements, Flexible Automation and Standards**

*Krishnendu Roy, Ph.D., The Robert A. Milton Chair and Professor, Biomedical Engineering; Director, Marcus Center for Cell Therapy Characterization Manufacturing (MC3M), Georgia Tech*

In this presentation, I will outline, using specific exemplars, how investment in identifying critical quality attributes (CQAs) and development of new technologies for in-line, rapid quality measurements would be critical for the field to move forward. I will also discuss how automation, especially flexible-adaptive automation and an industry-wide focus on developing pre-competitive standards will be key to our success in cell therapy CMC.

## INTERNATIONAL REGULATORY AND CMC STRATEGIES

**1:45 Regulatory Challenges and Strategies for Cell Therapies - US Perspective**

*Bernadette Keane, Ph.D., Principal, Keane Consultancy*

Cell therapies are substantially more complex than small molecule or biological approaches to medicine. This complexity poses challenges for both academic groups and companies developing cell therapies, as well as for regulators seeking to oversee this growing area of medicine. In this interactive session, we will discuss some of the common challenges and lessons learned along the way and explore how collaborations between industry and the regulators can help lead to successful translation and commercialization of cell therapies.

**2:15 Regulatory Aspects of Manufacturing and Control of Genetically Modified Cells**

*Matthias Renner, Ph.D., Scientist, Federal Institute for Vaccines and Biomedicines, Paul Ehrlich Institute*

In respect to manufacturing and quality control, genetically modified cells are considered to be most complex medicinal products. Regulatory aspects considering the fundamental steps in manufacturing and control of these medicinal products will be presented, and the regulatory framework for these products which are classified in the EU as advanced therapy medicinal products and are regulated centrally by the European Commission and the European Medicines Agency will be given.

**2:45 Refreshment Break**

**3:15 EU Regulatory Pathways for Standard and Accelerated Approval - Industry Perspective**

*Anthony Lodge, Ph.D., Manager, Regulatory Affairs, Chiesi*

In the EU, various regulatory pathways are available for taking cell and gene therapies (ATMPs) through clinical trials to commercial licensing, and the regulatory pathway taken will depend on the target patient population in which the ATMP will be used and the availability of existing therapies. The different pathways will be described in this presentation.

*Sponsored by* isoplexis

**3:45 Cell Therapy Product Characterization: Single Cell, Multiplexed Secreted Cytokine Analysis**

*Jonathan Chen, Single Cell Evangelist, IsoPlexis*

The characterization of cell therapy products and the ability to monitor product quality to support changes in the manufacturing process is challenging. This presentation introduces a new platform utilizing high parameter single cell secreted protein analysis to improve efficacy and immunotoxicity prediction.

**4:00 Key CMC Considerations for Cell Therapy Development and Approval**

*D. Allen Callaway II, MS, MBA, Associate Director, Global CMC Regulatory Affairs, Janssen (Pharmaceutical Companies of Johnson and Johnson)*

Each cell therapy development program involves the difficult task of managing health authority expectations and evolving guidances, while also adapting to internal program challenges around manufacturing scale-up, comparability, and appropriate analytical method selection, in order to predict and control product quality for pivotal trials. In this presentation, we will focus on the key CMC considerations for early and late phase development.

**4:30 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.

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

**7:00 End of Day**

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# Cell Therapy CMC, Quality and Analytics

## TUESDAY, AUGUST 22

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

## CHARACTERIZATION AND ANALYTICAL STRATEGIES

**7:55 Chairperson's Remarks**

*Christopher Bravery, Ph.D., Consulting Regulatory Scientist, Consulting on Advanced Biologicals Ltd.*

**8:00 Reliable Product Characterization by Flow Cytometry**

*Ruud Hulspas, Ph.D., Independent Consultant, Cellular Technologies Bioconsulting, LLC*

As cellular therapy entered the commercial sector, reliable and accurate product characterization has received extra attention. Although flow cytometry allows for extensive characterization of millions of cells, it is difficult, expensive and can introduce significant variability. This presentation provides an overview of flow cytometry in commercial cellular therapy, and discusses a number of practices that contribute to a better balance between the advantages and disadvantages of flow cytometry.

**8:30 Enumeration of CD34+ Cells by Flow Cytometry: USP's Perspective**

*Huiping Tu, Ph.D., Acting Senior Manager, Global Biologics, Science & Standard, United States Pharmacopeia*

What is the perspective of the enumeration of CD34+ cells from USP? USP Chapter <127> Flow Cytometric Enumeration of CD34+ Cells provides a single platform, standardized flow cytometric method for CD34+ cell enumeration based on ISHAGE protocol. The USP CD34+ Cell Enumeration System Suitability Reference Standard has been developed to assess the reagents and ensure the correct gating during data acquisition and analysis.

## POTENCY ASSAY DEVELOPMENT

**9:00 FEATURED PRESENTATION: Development of an Automated 28-Day Assay for T Cell Proliferation**

*Geoffrey Hodge, Ph.D., CTO, Unum*

Unlike traditional drugs, cell therapies like Unum's antibody-coupled T cell receptor (ACTR) platform technology actively expand and change after administration. Since traditional process development tools geared toward characterizing a static product are insufficient to fully understand the potential of cell therapies, Unum has designed a high-throughput 28-day "stress test," used to assess potential product and process changes, which reveals differences in performance not detected in short term *in vitro* assays.

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

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

**10:30 Allogeneic Cellular Cancer Vaccines: The Challenges of Characterization and Potency Assay Development**

*Sandra van Wetering, Ph.D., COO, DCPrime*

Characterization of cellular immunotherapy products in cancer is quite challenging, because induction of the cancer immunity cycle requires multiple functions, including activation of antigen-presenting cells and priming of naïve and memory T cells. DCPrime is developing allogeneic off-the-shelf DC vaccines based on its DC technology platform DCOne, and the talk will highlight which steps DCPrime is taking for its characterization and potency assay development for future clinical studies.

**11:00 Development and Implementation of a Cell-Based Potency Assay for a Dehydrated Human Tissue Product**

*Rebeccah Brown, Ph.D., Vice President, Global Regulatory Affairs, MiMedx Group, Inc.*

Numerous research studies on dehydrated human amnion/chorion membrane have demonstrated that it recruits and modulates the activity of cells to regrow, remodel and revascularize wounds. To determine that each lot of tissue maintains biological activity, a cell migration assay was selected for development into a Quality Control assay. The automation and validation activities required for successful implementation of a potency assay for an intrinsically variable product will be discussed.

**11:30 Potency Assay Development and Validation for Processed Human Nerve Allograft**

*Mark L. Friedman, Ph.D., Vice President, Regulatory Affairs and Quality Assurance, AxoGen® Corporation*

The regenerative potential of peripheral nerve allograft is due, in part, to the laminin coating of intact endoneurial tubes. A three-dimensional organotypic assay has been developed and validated which has shown to be able to assess the inherent regenerative potential of peripheral nerve allografts. This methodology can readily assess the potential efficacy of peripheral nerve allografts and provide a method to measure adjunctive regenerative therapies with peripheral nerve scaffolds.

**12:00 pm Cell and Gene Therapies: The Intricacies of Logistics on a Global Scale**

*Sponsored by* World Courier AmerisourceBergen

*James Connolly, Business Development Manager, Sales, World Courier, Inc.*

An in depth look at the challenges and unique transportation needs when conducting clinical trials in the cell and gene arena. From early stage, Phase I trials through to commercialization, we will review how early planning and foresight can greatly increase the chances of success as scale up is needed through the life of the trial stages and into the commercial market.

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

**1:15 Dessert Refreshment Break in the Exhibit Hall with Poster Viewing**

**1:55 Chairperson's Remarks**

*Damian Marshall, Ph.D., Head, Analytical Development, Non-Clinical Operations, Cell & Gene Therapy Catapult UK*

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# Cell Therapy CMC, Quality and Analytics

**2:00 Advanced Techniques for Immunotherapy Product Characterization**

*Damian Marshall, Ph.D., Head, Analytical Development, Non-Clinical Operations, Cell & Gene Therapy Catapult UK*

Autologous products such as gene-modified T-cell immunotherapies can have high levels of in-process variability which results in lower consistency of product manufacture. This presentation will demonstrate how advanced product characterisation and real-time in-process analytics can be applied to model variability and increase overall process control.

## PROCESS DEVELOPMENT AND CONTROL

**2:30 Autolus' Approach for Early-Stage CAR-T Cell Production**

*Emma Chan, Ph.D., Senior Scientist, Process Development, Autolus Ltd.*

Chimeric Antigen Receptor (CAR) T-cell therapies have shown great promise in hematological malignancies and are being developed using new technologies to target solid tumors, with the potential to offer a cure. Autolus, a private company spun-out by University College London in 2014, is developing cutting edge T-cell programming and manufacturing technology. Our aim is to optimize T-cell production processes to enable widespread distribution and commercialization of CAR T-cell technology.

**3:00 Manufacturing Control Strategies for Cell Therapies**

*Christopher Bravery, Ph.D., Consulting Regulatory Scientist, Consulting on Advanced Biologicals Ltd.*

For approval, it is necessary to demonstrate the manufacturing process is under control such that the product can be made at a consistent quality. To achieve this, the CQA need to be controlled through understanding and control of the critical process parameters and suitable in-process controls. The relative importance of these along with regulatory expectations will be discussed.

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

**4:15 US Approval of Three Rapid Microbiological Methods for MACI Product Release**

*John Duguid, Ph.D., Senior Director, Research & Development, Vericel Corporation*

Rapid detection of contaminants is essential for cell therapy products with short shelf lives. Integrating quality into the process through lot segregation, raw material qualification, environmental control, personnel training, and detailed procedures is critical because final results for conventional microbiological tests may not be available prior to product release or patient administration. US FDA approval of the MACI BLA in 2016 included three RMM product release assays for sterility, endotoxin, and mycoplasma.

**4:45 A Practical Guide to Process Development – An Academic Perspective**

*Patrick J. Hanley, Ph.D., Laboratory Facility Director, Cellular Therapy and Stem Cell Processing, Program for Cell Enhancement and Technologies for Immunotherapy, Division of Blood and Marrow Transplantation, Children's National Health System*

This presentation will focus on our experience translating cellular therapies from a basic science discovery at the bench into a Phase I clinical trial. Included in this presentation will be how to engage all members of the team, from clinicians to the manufacturing team, and design a system to best meet the needs of the process. These items include reagent qualification, cell selection, staffing, and product testing.

**5:15 Close of Conference**

**6:00 – 8:30 Recommended Dinner Short Course***

**SC5: Potency Assay Development for Cell and Gene Therapy Products**

** Separate registration required, see page 6 for details.*

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4TH ANNUAL

# Cell Therapy Manufacturing, Operations and Logistics

Commercializing Cell Therapies

## WEDNESDAY, AUGUST 23

**7:00 am Registration Open and Morning Coffee**

## PROCESS DEVELOPMENT, SCALE-UP AND COMMERCIALIZATION STRATEGIES

**8:05 Chairperson's Opening Remarks**
*Knut Niss, Ph.D., Vice President, Program Management, Mustang Bio*

**8:15 Commercialization Challenges in Cell and Gene Therapy**
*Devyn Smith, Ph.D., COO, Sigilon*
Differentiation, breakthrough, acceleration are the new buzzwords in the industry. How do we think about commercialization? Where are opportunities for new therapies? What are the challenges? There may be more answers than questions, but knowing the right questions to ask is important. This presentation will attempt to frame some of the key challenges and opportunities for new advanced therapies.

**9:00 Making Cell Therapy Process Changes: Why, How, and When?**
*Greg Russotti, Ph.D., Vice President, Cell Therapy Development and Operations, Celgene Corporation*
In order to make process changes for a cell therapy product, one must employ a combination of strong analytical tools, a thorough understanding of how the cell is intended to function as a therapy, detailed process characterization which elucidates how process parameters affect product attributes, and sound engineering principles to understand how the chemical and physical parameters of the process can be controlled to yield a comparable product after the process change. This presentation will discuss the reasons, methodologies, and timing for making process changes for cell therapy products.

**9:30 FEATURED PRESENTATION: Gene Editing and Synthetic Biology Toolbox for Pluripotent Stem Cell Therapies**
*Robert Deans, Ph.D., CTO, BlueRock Therapeutics*
BlueRock Therapeutics is a next-generation regenerative medicine company that plans to develop best-in-class induced pluripotent stem cell (iPSC) therapies to cure a range of diseases using an industry-leading platform. This presentation will outline BlueRock's strategy in cell therapy development based on latest stem cell technology in combination with superior cell differentiation protocols.

**10:00 Coffee Break in the Exhibit Hall with Poster Viewing**
Sponsored by ROCKLAND antibodies & assays

**10:45 Commercial Assessments beyond COGS: Are Allogeneic Therapies a Better Business Model?**
*Knut Niss, Ph.D., Vice President, Program Management, Mustang Bio*
In recent years, autologous cell therapies have come to the forefront of attention thanks to the emerging CAR-T technology. With the emergence of gene editing technologies, a new approach is being pursued in which T-cells are depleted of their TCR leading to "universal" T-cells that would not cause GvHD in an allogeneic recipient. This presentation will focus on some of the technical hurdles of generating allogeneic CAR-T cells as well as the potential challenges in the market place with such an approach.

**11:15 Best Practice for a Viable Academic Cell and Gene Therapy Program**
*Chy-Anh Tran, Associate Director, Operations, Stanford Laboratory for Cell and Gene Medicine, Stanford School of Medicine*
Stanford's Laboratory for Cell and Gene Medicine engages a wide facet of therapies that treat genetic diseases, attacks cancers, and equips viruses to replace faulty genes with healthy, functional copies. We provide the roadmap to clinical applications and our model will de-risk and effectively translate research innovation into exciting clinical therapies that will have a profound impact on the medical, scientific, and patient communities.

**11:45 Automated, Closed Manufacturing for Allogeneic Therapies**
Sponsored by MilliporeSigma
*Julie Murrell, Ph.D., Head of Cell Therapy Bioprocessing, MilliporeSigma*
The use of closed, single-use expansion and harvest systems can robustly expand and recover a variety of novel therapies. The inclusion of reagents that are animal origin free can lead to better yields and are supplied with a strong quality package. We will present data regarding ease of use, yield, viability and characterization for full solution expansion and harvest of manufactured cell therapies which are key enabling technologies for success in commercializing cell therapies.

**12:15 pm Luncheon Presentation: Next Generation Cell Expansion Technologies for Stem Cell Therapy**
Sponsored by CORNING
*Ryann Russell, Development Associate, Corning*

**1:00 Session Break**

## AUTOMATION, CLOSED SYSTEMS

**1:45 Chairperson's Remarks**
*Jeff Cram, Ph.D., Senior Scientist, Cellular Process Development and Manufacturing, bluebird bio*

**1:50 Benefits and Challenges Associated with Automation for Autologous Cellular Therapies: Why One Size Does Not Fit All**
*Jeff Cram, Ph.D., Senior Scientist, Cellular Process Development and Manufacturing, bluebird bio*
Early phase cell therapies rely on largely manual and partially closed systems that pose challenges to commercialization. Automating and closing systems is particularly challenging with autologous therapies due to small batch sizes and variable starting material. An appropriate automation strategy must also maintain manufacturing flexibility. I will review the pros and cons of some available cell processing devices as well as the benefits of a modular approach to automation.

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# Cell Therapy Manufacturing, Operations and Logistics

Commercializing Cell Therapies

**2:20 Innovative Solutions to Scaling Up and Out, Case Studies and Out-of-the-Box Thinking**

*Ohad Karnieli, Ph.D., MBA, CEO and Co-Founder, Atvio Biotech Ltd, Chair, Process and Product Development Subcommittee, International Society of Cellular Therapies*

As science evolves and cell therapies move from the bench to the clinic, a need for efficient and scalable solutions emerges. The commonly seen paths in the industry seem to be heading into a dead end. The traditional culturing technologies were not designed nor intended to culture cells at scale and a new and innovative thinking must emerge. The talk will describe and give tools and examples to such optional solutions.

**2:50 Approach to Late-Stage Process Development and Characterization of an Allogeneic Cell Therapy Product**

*Ravinder Bhatia, Ph.D., Director, Pharmaceutical Development and Manufacturing Sciences, Johnson & Johnson*

In this presentation, a case study will be presented on the considerations to select technologies to develop a robust, and scalable process for allogeneic cell therapy products. Also, a control strategy based on QbD principles to consistently meet product quality by controlling the raw materials attributes and process parameters will be discussed.

## GMP REQUIREMENTS, PROCESS VALIDATION AND LIFECYCLE MANAGEMENT

**3:20 GMP Considerations for Cell-Based Therapies**

*Trevor Deeks, Ph.D., Consultant, Deeks Pharmaceutical Consulting Services LLC*

This talk will consider the generic differences between the manufacturing processes of cell-based therapies and classical biotechnology processes and how these impact the GMP requirements, the quality systems and the process and final product controls. It will use examples and cases, both from cell therapy processes and from similar, more established biotechnology products, with similar challenges, such as live vaccines, to illustrate the challenges and how these can be overcome in practice.

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

**4:45 PLENARY KEYNOTE PRESENTATION**

*(See page 3 for details.)*

**6:00 Networking Reception in the Exhibit Hall with Poster Viewing**

**7:00 Close of Day**

## THURSDAY, AUGUST 24

**8:00 am Registration Open and Morning Coffee**

## CAR-T MANUFACTURING AND CHARACTERIZATION STRATEGIES

**8:25 Chairperson's Remarks**

*Anthony Davies, Ph.D., Executive Chairman, Dark Horse Consulting*

**8:30 Challenges and Solutions for Academic to Industry Translation of Personalized Engineered T Cell Therapies**

*Bruce Levine, Ph.D., Barbara & Edward Netter Professor, Cancer Gene Therapy, Perelman School of Medicine, University of Pennsylvania*

CAR T cells have demonstrated robust and durable clinical responses in relapsed and refractory malignancies. CAR T cell design includes elements of the receptor design, gene delivery to T cells, as well as the sourcing, manufacture, testing, delivery, and administration of the final CAR T cell product followed by clinical management of the patient. CAR T cells targeting new targets in hematologic malignancies and in solid tumors are underway and provide demonstration that it is possible to design immunity at will for therapeutic application.

**9:00 Product Characterization Options for Cell and Gene Therapies**

*Sadik H. Kassim, Ph.D., Vice President and Head, Cell Therapy Process and Analytical Development, Mustang Bio*

As "living drugs", cell therapies pose unique analytical characterization challenges; these challenges extend from the research bench to the cGMP manufacturing setting. This talk will review common analytical methods for cell therapies, specifically CAR T- and TCR-based therapies, with a specific emphasis on the limitations of current methods and desired areas of improvement.

*Sponsored by* MaxCyte

**9:30 Bench to Bedside Manufacturing: Implications of Choosing the Right Cell Engineering Platform**

*Madhusudan Peshwa, Ph.D., CSO, Executive Vice President, Cellular Therapies, MaxCyte*

Autologous, cell-based treatments have shown tremendous potential to address the unmet medical needs of thousands of people. Advancement of cellular therapies depends on the ability of researchers and manufacturers to deliver engineered cell-based therapeutic products that are safe and exhibit enhanced potency with resulting clinical efficacy. The ability to engineer such enhanced potency using non-viral, cGMP-compliant, automated and closed system manufacturing processes will represent a significant advantage. To outline how such a process might work, we will summarize the application of a scalable, cGMP-compliant, electroporation platform for engineering dendritic cells (DCs), NK cells and T cells for development of cellular immunotherapies targeting a range of malignancies and other disease applications.

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

**10:45 Process Development of CAR-T towards Commercialization**

*Marvin Lin, Ph.D., Principal Scientist, Cell & Gene Therapy and Process Sciences, Novartis Pharmaceuticals Corporation*

**11:05 Capacity Management Paradigms in CAR T Cell Therapy Manufacturing**

*Jon C. Gunther, Ph.D., Senior Engineer, Technical R&D, Juno Therapeutics*

Juno Therapeutics has developed a plant simulation of its global manufacturing network, and has the ability to modify various aspects of its manufacturing operations, such as process design, staffing totals, shift schedules, facility configuration, and activity prioritization. An overview of Juno's simulation and optimization methodology is presented here.

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# Cell Therapy Manufacturing, Operations and Logistics

Commercializing Cell Therapies

**11:25 Leveraging TALEN, Gene Edited CAR-T Platform to Industrialize Off-the-Shelf Allogeneic Cell-Based Pharmaceuticals**

*David Sourdive, Ph.D., Executive Vice President, Technical Operations, Cellectis*

TALEN®-mediated gene editing can turn CAR-T cell therapies into off-the-shelf pharmaceutical products widely and readily available to large patient populations. It is also the key to expand the use of CAR-T cells beyond the few targets and indications they have been successfully used so far. With the first gene-edited CAR-T product candidates now in clinic, and the first allogeneic CAR-T application, Cellectis is at the forefront of this endeavor.

**11:45 Manufacturing of Clinical Grade CAR-T NKR-2 THINK, Celyad First-in-Class Product Targeting Both Hematological and Solid Tumors**

*Sylvain Arnould, Ph.D., Director, Manufacturing and Production, Celyad*

Celyad is developing a unique CAR-T cell platform, using Natural Killer Receptor (NKR) transduced on to T lymphocytes. Platform targets a wide range of solid and hematological tumors. Celyad's lead candidate, CAR-T NKR-2, a CAR-T-Cell engineered express human NKR, NKG2D, and triggers cell killing through NKG2D binding to any of eight naturally occurring ligands overexpressed on more than 80% of tumors.

**12:15 pm Enjoy Lunch on Your Own**

**1:15 Dessert Refreshment Break in the Exhibit Hall and Last Chance for Poster Viewing**

**1:55 Close of Conference**

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# Gene Therapy

The Gene Therapy stream features two back-to-back conferences looking at the critical challenges facing the analytics, quality control and commercialization of vector-based and cell-based gene therapies, with dedicated sessions on AAV and lentivirus-based platforms as well as oncolytic viruses and gene editing therapies.

The first part of the week, Gene Therapy CMC and Delivery, looks at building an effective CMC development strategy followed by gene therapy potency assessment, stability, comparability and quality control. Part two, Gene Therapy Bioproduction, focuses on large-scale AAV and lentivirus process development, formulation, scale-up, product lifecycle management, industrialization and facility design and regulatory compliance.

**2017 GENE THERAPY TRACKS**

**AUGUST 23-24**

AGENDA Gene Therapy CMC & Analytics

**AUGUST 24-25**

AGENDA Gene Therapy Bioproduction

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# Gene Therapy CMC and Analytics

## WEDNESDAY, AUGUST 23

**7:00 am Registration Open and Morning Coffee**

## OPENING SESSION

**8:05 Chairperson's Opening Remarks**
*John Pieracci, PhD, Director, Purification, Biogen*

**8:15 KEYNOTE PRESENTATION: Analytical Testing Program for GMP Manufacturing Scale of AAV-Based Gene Therapy Vectors**
*Ernst Böhm, Analytical Product Owner, Analytical Development, Shire*
Production of AAV8-based gene therapy vectors requires an analytical strategy to enable process monitoring, process control, and release of clinical GMP batches. Implementation of an analytical method platform to assess key quality attributes was a priority. Potency assignment of the final product was most accurate when based on total capsid particle concentration, supported by vector genome concentration, degree of genome containing particles, and proof of efficacy in an *in vivo* model.

## CMC STRATEGIES FOR VECTOR-BASED GENE THERAPIES

**9:00 Global cGMP Strategy, Building a Global CMC Strategy**
*Ohad Karnieli, Ph.D., MBA, CEO and Co-Founder, Atvio Biotech Ltd; Chair, Process and Product Development Subcommittee, International Society of Cellular Therapies (ISCT)*
As therapies get closer to clinic, there is a growing need for global expansion. This global expansion not only results in the need for manufacturing scaling, but opens new challenges of meeting the different regulatory demands and supply limitations. Such challenges have to be considered early on in the products' lives and have to be planned carefully by building a global CMC strategy. The talk will discuss the challenges and provide case studies and examples for CMC strategies.

**9:30 CMC Focus during Innovation of Vector-Based Gene-Therapy Products**
*Arie van Oorschot, Ph.D., Senior Consultant, CMC, Xendo B.V.*
The application of gene-therapy products is diverse and developing rapidly. A few gene-therapy products are on the market, confirming that application of gene-therapy is feasible. Despite these successes, the general industrial experience and requirements can be considered limited. Typically, gene-therapy products are complex biologics and many iterations and a problem-solving attitude is required throughout development. To support the activities of multiple disciplines in parallel, an integrated CMC focus is essential.

**10:00 Coffee Break in the Exhibit Hall with Poster Viewing**
Sponsored by ROCKLAND antibodies & assays

## GENE THERAPY PRODUCT CHARACTERIZATION AND ANALYTICAL DEVELOPMENT

**10:45 Analytical Development and Testing Strategies for Viral Vectors Transitioning from Research to Non-Clinical and Clinical Stages**
*Eric Pastor, Principal Scientist, Biopharmaceutics Development, Sanofi US*
It is important to characterize and understand critical quality attributes of viral vector products throughout drug development. Here, we present analytical development strategies and paradigms as viral vectors transition from research to non-clinical and clinical stages. We will discuss lessons learned from past experiences as we move viral vector analytics from conception to validation and present ideas on how to accelerate method development.

**11:15 Qualification of AAV Vector Potency**
*Lyndi Rice, Ph.D., Director, Analytics, University of Pennsylvania*
The quantification of AAV vector potency over time and compared to other vectors is important for characterization for release and as part of stability programs. Potency assays are useful for determining transgene expression, activity and/or function *in vitro* or *in vivo*, and should be qualified for investigational drug product release. An example of potency assay development and qualification will be discussed.

**11:45 Using Manufacturing Software to Monitor Complex and Challenging Cell-Based Potency Assays for Gene Therapy Products**
Sponsored by ACF
*Patrick Dentinger, President, CEO, ACF Bioservices, an Absorption Systems Company*
Translational science includes many cell-based assays. Manufacturing is a dynamic process that requires monitoring. Our software tracks every step of a process from removal from the cell bank to manufacture and disposition of assay plates. We use the software for tracking a relative potency assay for an AAV gene vector.

**12:00 pm Analysis of Viral Vector Based Therapeutics: A Toolbox Approach**
Sponsored by FUJIFILM Diosynth Biotechnologies
*Cari Sadowski, Ph.D., Associate Principal Scientist, Group Leader, Virology Analytical Development, FUJIFILM Diosynth Biotechnologies*

**12:15 pm Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

**1:00 Session Break**

**1:45 Chairperson's Remarks**
*Michael Kelly, Ph.D., Director, Asset Leadership, Gene Therapy, Biogen*

**1:50 Qualification/Validation of Assays to Support the Release and Characterization of Recombinant Adeno-Associated Virus Clinical Trial Materials**
*Michelle Joubert, Ph.D., Scientist, Sanofi*
It is important to ensure that gene therapy viral vector assays are suitable for their intended use prior to releasing clinical trial materials. At Sanofi, this is accomplished by tailoring qualification or validation studies to the method types used at different stages of drug development. The strategy and results obtained from qualifying and validating methods for a gene therapy analytical paradigm will be discussed.

**2:20 Gene Therapy Potency Assay Development**
*Michael Hocquemiller, Ph.D., Senior Scientific Manager, Lysogene*

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# Gene Therapy CMC and Analytics

Mucopolysaccharidosis type IIIA (MPSIIIA) is a lysosomal storage disorder caused by mutations in N-sulfoglucosamine sulfohydrolase (SGSH), resulting in heparan sulfate (HS) accumulation and progressive neurodegeneration. Our approach is intracerebral gene therapy using AAV serotype rh.10 carrying the human SGSH cDNA. This talk will focus on the development of an *in vitro* potency assay for demonstrating batch-to-batch consistency of a gene therapy product.

**2:50 Development and Characterization of Mir-Attenuated Oncolytic Viruses**

*Michael Paglia, Ph.D., Senior Director, CMC Operations, Oncorus*

Development of a robust manufacturing process for therapeutic oncolytic herpes virus requires process understanding gained through process characterization. Process development and analytical strategies to ensure successful scale up and manufacturing for mir-attenuated oncolytic herpes virus will be presented.

**3:20 Demonstrating Comparability during Gene Therapy Tech Transfer**

*Scott Burger, M.D., Consultant, Advanced Cell and Gene Therapy Ltd.*

Changing the manufacturing site (tech transfer) should always include an assessment of comparability, however the ability to demonstrate this varies between early and late development. This talk will discuss common pitfalls and mistakes and highlight key aspects of the comparability exercise.

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

**4:45 PLENARY KEYNOTE PRESENTATION**
*(See page 3 for details.)*

**6:00 Networking Reception in the Exhibit Hall with Poster Viewing**

**7:00 Close of Day**

## THURSDAY, AUGUST 24

**8:00 am Registration Open and Morning Coffee**

## QUALITY CONTROL OF GENE THERAPIES

**8:25 Chairperson's Remarks**

*Xiaohui Lu, Ph.D., Senior Scientist, Analytical Development, Biogen*

**8:30 The Quest for Accurate AAV Capsid Quantification**

*Xiaohui Lu, Ph.D., Senior Scientist, Analytical Development, Biogen*

AAV capsid titers are often determined using commercial ELISA assay kit. However, the reference standard in the commercial kits subject to batch-to-batch variations, and its value assignment can also be improved. In this case study, we evaluated alternative approaches, and generated internal reference standard with orthogonally determined concentration. This customized assay will enable reliable capsid titer quantification over long terms.

**9:00 Analytical issues for AAV gene therapy products: vector genome titer and full/empty viral particles quantification**

*Christine Le Bec, PhD, Head of Analytical Development, Genethon*

Selected analytical assays were developed to assess the vector productivity, vector purity, biological activity/potency. The quantitative PCR (qPCR) is the current gold method of titrating AAV genomes. The Droplet Digital PCR (ddPCR), a new technology which has been designed for accurate DNA quantification, could improve titer determination. Comparison between these two methods will be discussed. The presentation will also cover methods to determine the ratio of full/empty viral capsids

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

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

## QUALITY CONTROL OF GENE THERAPIES

**10:45 Insights in Measuring DNA Impurities by Real-Time PCR in Clinical AAV Vectors**

*Sebastiaan van Zalen, Ph.D., QC Manager, Clinical Vector Core, The Raymond G. Perelman Center for Molecular and Cellular Therapies, Children's Hospital of Philadelphia*

Purified AAV vectors contain measurable levels of process-related DNA impurities. Residual levels of plasmid and host cell DNA in the vector can have direct product safety implications and therefore have to be accurately measured. We compared suitability of currently-available quantitative PCR platforms for measurement of DNA impurities in AAV vectors within clinical titer range and assessed other contributing factors such as titer, vector genome length, serotype, and manufacturing method.

**11:15 Identity Assessment of AAV Preparations**

*Simon Pacouret, Research Fellow, Grousbeck Gene Therapy Center, Massachusetts Eye and Ear, Harvard Medical University; INSERM UMR 1089*

Viral vector preparations for gene therapy are complex biologics. With the steady progression of the adeno-associated viral vector (AAV) platform, identity assessment of vector preparations is key. Here, we will review the available assays to assess identity on a genomic, protein, and particle level. In addition, we will describe our work on AAV-ID, a time- and cost-effective method to establish lot-to-lot identity information on formulation, protein, and particle identity.

**11:45 The Quest for Accurate AAV Capsid Quantification**

*Xiaohui Lu, Ph.D.,Senior Scientist, Analytical Development, Biogen*

AAV capsid titers are often determined using commercial ELISA assay kit. However, the reference standard in the commercial kits subject to batch-to-batch variations, and its value assignment can also be improved. In this case study, we evaluated alternative approaches, and generated internal reference standard with orthogonally determined concentration. This customized assay will enable reliable capsid titer quantification over long terms.

**12:15 pm Enjoy Lunch on Your Own**

**1:15 Dessert Refreshment Break in the Exhibit Hall and Last Chance for Poster Viewing**

**1:55 Close of Conference**

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# Gene Therapy Bioproduction

Developing Scalable, Cost-Effective Gene Therapy Manufacturing Processes

## THURSDAY, AUGUST 24

**11:30 am Registration Open**

**12:15 pm Enjoy Lunch on Your Own**

**1:15 Dessert Refreshment Break in the Exhibit Hall and Last Chance for Poster Viewing**

## PROCESS DEVELOPMENT STRATEGIES FOR LENTIVIRUS-BASED PROCESSES

**1:55 Chairperson's Remarks**

*Lance Weed, Ph.D., Vice President, Operations, uniQure*

**2:00 KEYNOTE PRESENTATION:**

**Managing Challenges in Late Phase Process Development for Cell and Gene Therapies**

*Michele Myers, Ph.D., Senior Director, Validation and Lifecycle Management, Cell and Gene Therapy, Platform Technology & Sciences, GlaxoSmithKline*

To date, GSK has optioned three programs as part of its strategic collaboration agreement with the Telethon Institute for Gene Therapy to develop autologous *ex vivo* gene therapies for the treatment of rare diseases. This talk will describe the challenges associated with development and implementation of late-stage/post-approval process changes and technology transfer of these programs. The approach to comparability and process qualification will be discussed.

**2:45 Lentivirus Development and Scale-Up**

*Jesse Milling, Scientist II, bluebirdbio*

Lentiviral vectors are an ideal platform for indications requiring long-term, stable expression, but the production processes have historically been limited by scale. This presentation will focus on the evaluation of platforms for the next-generation manufacturing process, with the guiding principles of preserving the comparability of the lentiviral product profile.

**3:15 Strategies to Deliver Scalable and Reliable Lentiviral Vector Biomanufacturing**

*Jeffrey Bartlett, Ph.D., CSO, Calimmune Inc.*

Large-scale clinical production of lentiviral vectors (LV) using current good manufacturing practice (cGMP) methods comes with significant challenges. We have established the Cytegrity stable cell line system for LV bioproduction and have defined key process, quality and regulatory parameters needed to achieve desired productivity and quality across multiples scales and different bioproduction systems. This approach has allowed the production of LV required for Phase I and II clinical trials, while paving the way for future commercialization.

*Sponsored by* BIA Separations

**3:45 High Resolution Monolithic Columns - Enabling Tool for Understanding Viral Structures and Their Purity**

*Ales Strancar, CEO, BIA Separations*

Monolithic resins with open channels and no diffusive pores enabled the HPLC to be extensively applied for viral structures separations. HPLC columns based on CIM monolithic chromatographic supports are not only able to determine the ratio of full/empty viral capsids but can further separate and analyse subpopulations of the capsids.

**4:00 Refreshment Break**

## PROCESS DEVELOPMENT STRATEGIES FOR OTHER VIRUSES

**4:15 Retroviral Vector Process Development for CAR T Applications**

*Paulo Fernandes, Senior Scientist, Process Development, Autolus*

While retroviral vectors are one of the preferred choices for stable gene expression, the manufacture of these vectors is still limited in titer and quality. This presentation will focus on the process development efforts at Autolus to manufacture retroviral batches in sufficient amounts and with the right quality attributes for T-cell transduction and engineering.

## DEVELOPMENT AND PRODUCTION CHALLENGES FOR GENE EDITING THERAPIES

**4:45 FEATURED PRESENTATION:**

**Development and Production Challenges for CRISPR Gene-Edited Products**

*Kenneth LeClair, Ph.D., Vice President, Technical Development and Manufacturing, Editas Medicine*

This presentation will provide a high-level overview of the considerations involved in the development of CRISPR/Cas9-based gene therapy products. The product development life cycle will be reviewed, starting from product candidate selection, developability assessments, and final product manufacturing. Examples of direct-inject viral vector therapies and of *ex vivo* engineered cell products will be presented.

**5:15 Close of Day**

**6:00 – 9:00 Recommended Dinner Short Course***
**SC9: Transient Protein Production in Mammalian Cells**

** Separate registration required, see page 6 for details.*

## FRIDAY, AUGUST 25

**8:00 am Registration Open and Morning Coffee**

## PROCESS DEVELOPMENT STRATEGIES FOR AAV-BASED PROCESSES

**8:25 Chairperson's Remarks**

*Johannes C.M. van der Loo, Ph.D., Director, Clinical Vector Core, The Raymond G. Perelman Center for Molecular and Cellular Therapies, Children's Hospital of Philadelphia*

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# Gene Therapy Bioproduction

Developing Scalable, Cost-Effective Gene Therapy Manufacturing Processes

**8:30 KEYNOTE PRESENTATION:**
**Considerations and Challenges When Establishing a New Manufacturing Facility**
*Lance Weed, Ph.D., Vice President, Operations, uniQure*

Over the past four years, uniQure has invested more than $25 million in designing, constructing and equipping its 55,000-square foot facility with state-of-the-art laboratories and commercial-scale production capabilities. This presentation will discuss the challenges in establishing a new manufacturing facility from scratch, and what small companies should consider when deciding whether to build their own manufacturing capability or use contract manufacturing.

**9:00 Manufacturing Considerations for AAV Gene Therapies**
*K. Reed Clark, Ph.D., Senior Vice President, Pharmaceutical Development, Dimension Therapeutics*

This presentation will discuss our approaches for scalable manufacturing to inform late-stage manufacturing of AAV-based gene therapy products. Lessons learned in the development of mammalian-based production platforms will be highlighted and the necessary analytics to support efficient process development discussed.

**9:30 rAAV Vector Production in the Baculovirus/Sf9 Platform and in HEK293 Suspension Cell System**
*David Dismuke, Director, Vector Production, Voyager Therapeutics*

Gene therapy vectors based on recombinant adeno-associated virus (rAAV) have continued to demonstrate their utility as effective, dependable, and safe tools for gene delivery. They have been used extensively in clinical trials to replace or silence genes in a variety of tissues, including the eye, brain, muscle, and the liver. As the success of AAV gene therapy has grown, so have the doses and demand for the vectors. To supply the high titers required for late-stage clinical trials and expected commercial demands, several manufacturing platforms have been developed, including the baculovirus/Sf9 platform and transient transfection in HEK293 suspension cells. While both of these systems are capable of generating high quality AAV vectors, the baculovirus/Sf9 system offers higher yields and fully scalable unit operations

**10:00 Networking Coffee Break**

**10:30 Scalable and Cost-Effective Production of Diverse Recombinant AAVs**
*Mark Fox, Ph.D., Director, Process Sciences, 4D Molecular Therapeutics*

rAAVs have become a well-accepted gene therapy delivery detail, with an increasing diversity of serotypes and variants entering clinical testing. But many AAV manufacturing processes still use labor-intensive, expensive, non-scalable and cGMP compliance-resistant unit operations. 4D has adopted a strategic approach to process development for its portfolio of AAV products. We will discuss this cost-effective, scalable and compliant manufacturing platform and its potential breadth of application.

**11:00 Advantages and Challenges of Early Phase Clinical Manufacturing in an Academic Setting**
*Johannes C.M. van der Loo, Ph.D., Director, Clinical Vector Core, The Raymond G. Perelman Center for Molecular and Cellular Therapies, Children's Hospital of Philadelphia*

The Clinical Vector Core at the Children's Hospital of Philadelphia has manufactured pre-clinical- and clinical-grade AAV and lentivirus-based custom viral vector products in support of early phase clinical studies. Manufacturing in an academic non-profit setting, which provides significant advantages to new investigators, includes unique challenges that require consideration. Awareness of these challenges helps both manufacturers and investigators streamline the process of bringing new gene therapy products to the clinic.

**11:30 Separation of Virus, VLP and Extracellular Particles**
*Alois Jungbauer, Ph.D., Professor, Institute of Biotechnology, University of Natural Resources and Life Sciences (BOKU)*

Downstream processing of enveloped bio-nanoparticles is very challenging due to biophysical and structural similarity between correctly assembled particles such as VLP, viruses, exosomes and contaminating vesicular particles are present in the feedstock. Direct capture by connective media or flow through chromatography are used in connection with linear gradient elution to separate the products from other vesicles. Also advanced analytics will be addressed to discriminate the different particles.

**12:00 pm Sponsored Presentation** *(Opportunity Available)*

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

**1:15 Session Break**

## SCALING-UP AND INDUSTRIALIZING GENE THERAPIES

**1:25 Chairperson's Remarks**
*Norman Goldschmidt, President, Genesis*

**1:30 Development and Optimization of a Serotype-Independent Method of Adeno-Associated Virus Harvest and Purification**
*Bryan Piras, Ph.D., Senior Scientist II, Process Development, Therapeutics Production and Quality, St. Jude Children's Research Hospital*

We assessed commercially available scalable single-use chromatography membranes for their ability to capture AAV vectors directly from cell culture media and lysate. We developed a simple technique that integrates release of cell-associated AAV particles followed by capture and recovery on a hydrophobic interaction chromatography membrane. This process is serotype-independent and provided efficient capture and recovery of AAV1, AAV3-like, AAV5, and AAV8 particles from cell culture media and cell lysate.

**2:00 AAV Vectors: From Discovery to Large-Scale Clinical Manufacturing: An Academic Success Story**
*Nathalie Clément, Ph.D., Associate Director and Associate Professor, Powell Gene Therapy Center, Pediatrics, University of Florida*

A brief history of AAV vectors at the University of Florida from their first engineering to the first clinical trials will be presented. Current manufacturing protocols developed at the Powell gene therapy will be discussed and compared, with a strong emphasis on the recently implemented large-scale production platform in suspension cells using HSV-system. Data will cover yields, quality, potency, purity and other CMC requirements for GMP manufacturing.

**2:30 Formulation Development for AAV Gene Therapy Application**

*Tanvir Tabish, Head, Drug Product Development for Gene Therapy, Device and Combination Products, Shire*

A set of formulations was screened. One was found to stabilize the AAV based product for at least 5 months when stored frozen, and for at least 4 months when stored at +5°C. No visible particles together with no significant loss of infectivity or total particle titre was observed. SDS-PAGE and SEC did not show significant chemical or physical degradation. Adsorption studies did not reveal any loss with contact materials.

**3:00 Engagement with FDA and Facility Design for Cell and Gene Therapies**

*Norman Goldschmidt, President, Genesis*

*Johannes C.M. van der Loo, Ph.D., Director, Clinical Vector Core, The Raymond G. Perelman Center for Molecular and Cellular Therapies, Children's Hospital of Philadelphia*

As cell and gene therapies are moving forward to becoming mainstream treatment modalities, the relationship of hospitals and universities with the FDA is rapidly evolving. Organizations producing phase 2 and later clinical therapies are receiving more attention and scrutiny from regulators. This session will look at the general principals of approvable cGMP facility design and one organization's approach to proactively engaging with FDA during the design process to manage risk and allow incorporation of FDA's latest thinking in facility design at an early stage.

**3:30 End of Conference**

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# Manufacturing

A new stream this year, the weeklong Manufacturing stream covers some of the most important aspects of process development. The stream combines three key manufacturing concerns: 1) Technology – Continuous Processing, 2) Process – Manufacturing Efficiencies and Process Improvement, and 3) CMC – CMC Strategies for Antibody-Drug Conjugates, and showcases case studies and latest developments in the respective fields to help companies improve their process, manufacturing and CMC strategies.

2017 MANUFACTURING TRACKS

**AUGUST 21-22**

AGENDA Continuous Processing in Biopharmaceutical Manufacturing

**AUGUST 23-24**

AGENDA Manufacturing Efficiencies & Process Improvement

**AUGUST 24-25**

AGENDA CMC Strategies for Antibody-Drug Conjugates

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# Manufacturing Efficiencies and Process Improvement

**FOR CONTINUOUS PROCESSING IN BIOPHARMACEUTICAL MANUFACTURING AGENDA** taking place on Monday, August 21 and Tuesday, August 22, **please see pages 19-21 for more details.**

## WEDNESDAY, AUGUST 23

**7:00 am Registration Open and Morning Coffee**

**8:05 Chairperson's Opening Remarks**

*Chava Kimchi-Sarfaty, Ph.D., Research Chemist, Principal Investigator, Division of Plasma Protein Therapeutics, Office of Tissues and Advanced Therapies, FDA | CBER | OTAT*

**8:15 KEYNOTE PRESENTATION:**

**National Medical Countermeasure Response Infrastructure Overview**

*Joseph Figlio, Program Manager, Centers for Innovation in Advanced Development & Manufacturing [CIADM], Biomedical Advanced Research & Development Authority [BARDA], Office of the Assistant Secretary for Preparedness & Response [ASPR], U.S. Department of Health & Human Services*

*Timothy Belski, Joint Product Director, Medical Countermeasures Advanced Development & Manufacturing Capabilities [MCM-ADMC], Joint Project Manager for Medical Countermeasure Systems [JPM-MCS], Joint Program Executive Office for Chemical and Biological Defense [JPEO-CBD], U.S. Department of Defense*

Over the last several years, the U.S. government has worked closely with the biopharmaceutical industry to establish a set of capabilities in order to address the nation's needs for medical countermeasures. Working through these public-private partnerships, a core set of these capabilities leverage innovative equipment and infrastructure design to enable agile and flexible advanced development and manufacturing under cGMPs (e.g. multi-product biopharmaceutical facilities, mobile clean rooms, single use technology).

## LEVERAGING INNOVATIONS IN EQUIPMENT, INFRASTRUCTURE AND FACILITIES

**9:00 The Enterprise: Biomanufacturing's Vehicle for Achieving Manufacturing Efficiency**

*Jeff Odum, CPIP, Global Technology Partner, Strategic Manufacturing Concept Group, NNE PharmaPlan*

Creating strategic manufacturing assets for diverse product portfolios and new technology platforms requires development of an enterprise approach to biomanufacturing and optimization of the key enterprise elements. The key drivers of flexibility, agility, efficiency, and utilization have differing approaches within the enterprise model. This presentation will define the key elements of the approach and discuss case examples of attribute definition and risk-focused design execution.

**9:30 Adaptable Facilities to Meet the Needs of New, Multiple Products with Varied Manufacturing Processes**

*David M. Marks, PE, President & Principal Consultant, DME*

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

*Sponsored by* ROCKLAND antibodies & assays

**10:45 10:45 Smart Design for an Efficient Facility with a Validated Disposable System**

*Jason Li, Vice President, Downstream Process & Technology Transfer, Genor Biopharma Co., Ltd.*

Disposable systems have been proven to ensure efficient and flexible production of biologics. Both upstream and downstream processing case studies will be presented. In addition, the pros and cons for application of disposable as stainless steel systems will be compared in further detail.

**11:15 Improving Efficiency, Evaluating Improvements: A Standardized Economic Cost Modeling Approach**

*Andrew Sinclair, Founder & President, Biopharm Services Ltd.*

Rapid evaluation of technology options needs to be introduced early in product/process development, both for individual products and in development of improved manufacturing platforms. A foundation supporting such efforts is the use of economic analysis that allow the impact of a technology to be evaluated across a complete end-to-end platform process. This presentation evaluates the approaches and illustrates the potential of the standardized approach to look at those technologies that could impact on the next generation CHO MAb-production platform. It will focus on the potential or otherwise of the N-1 concentrated seed and potential of a novel Membrane Hydrogel Capture Step.

**11:45 Sponsored Presentation** *(Opportunity Available)*

**12:15 pm Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

**1:00 Session Break**

## ADAPTING PLATFORM STRATEGIES TO IMPROVE EFFICIENCIES FOR NEXT-GENERATION THERAPIES

**1:45 Chairperson's Remarks**

*Steven Cook, Head, Global Biologics Supply Operations, AstraZeneca*

**1:50 FEATURED PRESENTATION:**

**Exosome Production: Limitations of the Current Toolbox and Strategies to Overcome Them**

*Michael Mercaldi, Ph.D., Director, Purification Process Development and Manufacturing, Codiak Biosciences*

Exosomes have emerged as a therapeutic platform that could allow for the development of highly potent and directed therapeutics. The current state of exosome bioprocessing is limiting and will need to be improved to meet the potential future demands of these therapeutics. In this presentation, the potential of exosome-based therapeutics and the bioprocessing technologies for their future commercialization will be discussed in the context of the capabilities and limitations of the existing biomanufacturing platforms.

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# Manufacturing Efficiencies and Process Improvement

**2:20 The Rewards and Risks of Using New Platform Technologies for Improved Therapeutic Protein Drugs**

*Chava Kimchi-Sarfaty, Ph.D., Research Chemist, Principal Investigator, Division of Plasma Protein Therapeutics, Office of Tissues and Advanced Therapies, FDA | CBER | OTAT*

Recently approved recombinant protein therapeutics have been developed to treat patients with a wide variety of clinical indications, and the latest advances in protein engineering technologies have allowed drug developers and manufacturers to fine tune and exploit desirable functional characteristics of proteins of interest while maintaining product safety and/or efficacy. The talk will highlight the emerging trends and approaches in protein drug development using examples of therapeutic proteins approved by the U.S. FDA.

**2:50 Challenges and Opportunities in Implementing Continuous/Semi-Continuous Downstream Processing**

*Lynn Conley, Biopharmaceutical Consultant*

With cell culture titers and productivity increasing in the last decade, pressure is placed on downstream purification to look at alternative strategies to meet the demand of biotech products with high dose requirements. Even when the upstream process is not continuous (perfusion based), adopting a more productive continuous/semicontinuous downstream process can be of significant advantage. This presentation will review the various processing options for biomolecules and discuss the enabling technologies, its challenges and opportunities.

**3:20 PANEL DISCUSSION: Developing and Manufacturing Next-Generation Therapies**

*Moderator:*

*Michael Mercaldi, Ph.D., Director, Purification Process Development and Manufacturing, Codiak Biosciences*

*Panelists:*

*Chava Kimchi-Sarfaty, Ph.D., Research Chemist, Principal Investigator, Division of Plasma Protein Therapeutics, Office of Tissues and Advanced Therapies, FDA | CBER | OTAT*

*Lynn Conley, Independent Consultant*

- Limitations of current technologies
- How to select the proper regulatory pathway
- How to "break" out of the mAb toolbox
- Lifecycle development approach

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

**4:45 PLENARY KEYNOTE PRESENTATION**

*(See page 3 for details.)*

**6:00 Networking Reception in the Exhibit Hall with Poster Viewing**

**7:00 Close of Day**

## THURSDAY, AUGUST 24

**8:00 am Registration Open and Morning Coffee**

## ACHIEVING EFFICIENCIES IN PROCESS DEVELOPMENT, SUPPLY CHAIN AND TECH TRANSFER

**8:25 Chairperson's Remarks**

*Lynn Conley, Biopharmaceutical Consultant*

**8:30 Advancing Continuous Process Monitoring and Real-Time Analytics for Biologics Manufacturing**

*Gloria Gadea-Lopez, Director, Shire*

*Robert Dimitri, Associate Director, Process Analytics, Shire*

Technical teams across the Shire Lexington site rely on the availability of process data from multiple sources to conduct continuous process monitoring activities, resolve investigations, and identify areas of improvement. This presentation will describe the successful implementation and use of a comprehensive, integrated, GMP data analytics system and the benefits that its use has provided to the organization.

**9:00 Scheduling and Optimization of Process Activities in Facilities with Disposable Technologies**

*Mark Maselli, Senior Engineer, Single Use Systems, Shire*

*John Maguire, Associate Director, Manufacturing Systems, Shire*

The use of disposable equipment for production is expanding significantly in the biotech industry. As a result, companies need to adapt their manufacturing systems accordingly and accommodate the specific needs of this technology. In this presentation, the speakers will discuss the impact to the configuration of finite scheduling tools and the need for a comprehensive program for the management of single use systems at Shire-Lexington site.

**9:30 Process Development to Mitigate Supply Chain Risks**

Sponsored by Patheon

*John Ward, Vice President, Engineering, Patheon*

The planning process for launching a new product can be daunting for biologics companies. Critical factors such as inaccurate demand forecasts, process development variability and market timing must all be considered, making the supply chain planning process for biologic drug substance difficult at best. This presentation will evaluate some of the production options available as well as processes that will maximize an organization's ability to maintain flexibility on the path to commercialization.

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

**10:45 End-to-End Supply Chain Management for Complex, On-Demand Manufacturing and Distribution Networks**

*Steven Cook, Head, Global Biologics Supply Operations, AstraZeneca*

Discussion will focus on the challenges of managing a dynamic global biologics supply chain and how to build in flexibility and manage agile delivery in a fast growing, new product introduction environment. Low volume, high value biologics are changing the healthcare landscape across the globe. New therapies bring uncertainty of demand and increasing pressures on manufacturing and supply chain to meet conflicting needs for speed, high customer service and costs.

**11:15 Integrating Single-Use PAT Tools with Lean Manufacturing Principles at the Seed Stage - Challenges and Opportunities**

*Jose R. Vallejos, Ph.D., Manufacturing Cell Culture Scientist, Manufacturing Sciences & Technology, MedImmune*

The potential benefits of implementing PAT tools at the seed stage (in a GMP environment) are lean manufacturing operations, reduced risks from bioburden/contamination, and mitigation of risks associated with tech/process transfer. Some challenges that can contribute to the slow

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## Manufacturing Efficiencies and Process Improvement

implementation of PAT tools at the seed stage include a lack of understanding on how to go about implementing PAT tools, a lack of business strategy alignment between PD and Operations, and a lack of familiarity/understanding of the biotech industry needs and priorities.

**11:45 Bridge Building: How to Manage Complex Technology Transfers**

*Jacob Jensen, Senior Manager, Global Program Management, Biogen Denmark*

- What are the considerations required to ensure a smooth transfer of operations from R&D to manufacturing?
- Evaluation of critical aspects to ensure event-free manufacturing
- Discovering the importance of cross-functional communication and collaboration to promote successful routine biomanufacturing operations

**12:15 pm Enjoy Lunch on Your Own**

**1:15 Dessert Refreshment Break in the Exhibit Hall and Last Chance for Poster Viewing**

**1:55 Close of Conference**

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# CMC Strategies for Antibody-Drug Conjugates

## THURSDAY, AUGUST 24

**11:30 am Registration Open**

**12:15 pm Enjoy Lunch on Your Own**

**1:15 Dessert Refreshment Break in the Exhibit Hall and Last Chance for Poster Viewing**

## KEYNOTE PRESENTATIONS

**1:55 Chairperson's Remarks**
*Heidi J. Hoffmann, Ph.D., Senior Director, Supply Chain/CMC, Sutro Biopharma*

**2:00 Development and Manufacture of a Novel Drug-Linker Enabling High-DAR ADCs**
*Michael J. Kaufman, Ph.D., Senior Vice President, CMC, Mersana Therapeutics*
Recently, Mersana Therapeutics has announced the commencement of clinical trials with XMT-1522, a HER2-directed ADC possessing a DAR of 12–15 while maintaining acceptable PK and drug-like properties in preclinical models. In this talk, the process development and manufacture of Fleximer-based ADCs are discussed, with particular emphasis on unit operations in the manufacturing process that provide control of heterogeneity and promote lot-to-lot consistency.

**2:45 Development and Manufacturing of SYD985, a Duocarmycin-Based ADC**
*Aad van de Leur, MSc, COO, Biopharmaceuticals Development, Synthon Biopharmaceuticals*
Synthon is developing SYD985, a Duocarmycin-based ADC which is in Phase I clinical development. To allow clinical studies, a conjugation process was developed. Challenges and different approaches to develop a robust conjugation process will be presented. In addition the implications on facility design to handle larger batch sizes to meet standards for safe, effective and reliable manufacturing will be discussed. Clinical data of our dose escalation study will be presented.

## SUPPLY CHAIN MANAGEMENT AND TECH TRANSFER TO CMO

**3:15 Best Practices in Externalization of the ADC Supply Chain**
*Vincent Turula, Director, External Supply, Biotherapeutics Pharmaceutical Sciences, Worldwide R&D, Pfizer, Inc.*

**3:45 Sponsored Presentation** *(Opportunity Available)*

**4:00 Refreshment Break**

**4:15 Analytical Testing Strategy for Kadcyla® Cleaning Validation in Support of a Drug Product Transfer to CMO**
*Lan Dai, Ph.D., QC Associate Scientist, MMTech Analytical Chemistry & Lifecycle Management, Global QC Network, Genentech Inc., A Member of The Roche Group*
Cleaning validation bottlenecks manufacturing site transfers. The complexity is increased for ADC products, because in addition to meeting requirements of general TOC tests, the presence of cytotoxic residues must also not exceed a pre-defined Maximum Allowable Carryover level after equipment cleaning. The design of QC testing/validation strategy is focused on linking analytical testing to the cleaning process/facility design and aligned with health authority, the company and the CMO's compliance practice.

**4:45 Sourcing for the Right CMOs and Managing Complex Supply Chain Networks for Antibody Drug Conjugates**
*Brian Clark, Principal, GMP Operations Consulting*
ADC manufacturing involves some of the most complex supply chains in the biopharmaceutical business. This session will review the challenges with, and strategies for, CMO selection for the various components of ADCs. It will also discuss approaches for simplifying and managing these complex networks.

**5:15 Close of Day**

## FRIDAY, AUGUST 25

**8:00 am Registration Open and Morning Coffee**

## ANALYTICAL AND FORMULATION STRATEGIES FOR ANTIBODY-DRUG CONJUGATES

**8:25 Chairperson's Remarks**
*Brian Clark, Principal, GMP Operations Consulting*

**8:30 Use of Slope Measurement for Concentration and DAR Determination of Antibody-Drug Conjugates**
*Michael Fleming, MS, Sr. Scientist, Analytical & Pharmaceutical Sciences, ImmunoGen, Inc.*

**9:00 Analytical and Characterization Strategies for Pfizer's Early Stage ADC Development**
*Verl Sriskanda, Ph.D., Principal Scientist, ARD, Biotherapeutics Pharmaceutical Sciences, Pfizer*
- Molecular assessment for ADCs
- Early stage analytical characterization road maps for ADCs
- Analytical method development strategies for early stage ADCs

**9:30 Developing an Efficient, Robust and Scalable Conjugation Process for a Bispecific ADC**
*Sanjay Nilapwar, Ph.D., Scientist, Purification Development, MedImmune*

**10:00 Networking Coffee Break**

**10:30 Analytical and Process Development of a Lyophilized ADC**
*Lisa Hardwick, Research Scientist, Baxter Healthcare*
While the development of an aqueous solution formulation may be preferred over a lyophilized product, it is useful to initially pursue a dual path and develop drug product formulations for both a sterile solution and a freeze-dried solid presentation, ultimately choosing the most successful candidate for final development. This presentation will provide an overview of the development process, useful analytical development tools, and lyo cycle optimization.

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# CMC Strategies for Antibody-Drug Conjugates

**11:00 Critical Quality Attribute Assessment of Antibody-Drug Conjugates: A Case Study**
*Hangtian Song, Ph.D., Senior Scientist, Bristol-Myers Squibb*

**11:30 PANEL DISCUSSION: Regulatory Complexity for Registration of an ADC**
*Moderator: Aad van de Leur, MSc., COO, Biopharmaceuticals Development, Synthon Biopharmaceuticals*

- Will expectations for information provided for the linker-drug and mAb be the same as for a Drug Substance?
- How to set specifications for Linker Drug assuming the conjugation process will impact these impurities
- Taking into account the complex and long lasting supply chain for an ADC multiple process changes could occur during development of the complete process. How will changes in manufacturing Linker-Drug or mAb impact qualification status of DS and DP?
- Is there a need to have a cell based potency assay for a mAb to be used in an ADC process?

**12:00 pm Sponsored Presentation** *(Opportunity Available)*

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

**1:15 Session Break**

## PROCESS SCALE-UP AND MANUFACTURING

**1:25 Chairperson's Remarks**
*Lisa Hardwick, Ph.D., Research Scientist, Baxter Healthcare*

**1:30 In-House Production and Scale-Up of Site-Specific ADC for Phase I Trials**
*Sean Hu, Ph.D., CEO, Dophen Biomed*

To speed up Dophen's own site-specific ADC program and take advantage of our one-pot reaction of antibody drug conjugation, we have developed our in-house pilot ADC production process for pre-clinical GLP tox and Phase I clinical material supply. This process is safe, scalable, robust and quick to significantly reduce the time needed from research to Phase I. A typical batch takes about a week to complete without counting the time needed in logistics planning.

**2:00 Strategy to Advance ARX788 ADC from Development to Clinical Manufacturing and Lessons Learned for Future ADC Program at Ambrx**
*Jon Strauss, MSc., Senior Scientist, Process Sciences, Ambrx Inc.*

CMC strategies for global filing can be very challenging because different cGMP and clinical filing regulations are applied in different countries/regions. This presentation will provide Ambrx's view on appropriate CMC strategies developed in ARX788 program which is currently in the global multi-center Phase I clinical study.

**2:30 Development and Manufacturing Strategies for Antibody-Drug Conjugates Using XPressCF™ Platform Technology**
*Heidi J. Hoffmann, Ph.D., Senior Director, Supply Chain/CMC, Sutro Biopharma*

Sutro has developed Xpress CF™ as a protein expression platform based on proprietary *E. coli* cell extract (Xtract CF™), which utilizes the transcription/translation machinery of *E. coli* to produce therapeutic proteins in an open cell-free system. The presentation will describe how Sutro uses this technology for discovery, optimization, and production of Antibody-Drug Conjugates (ADCs). The presentation will also include discussion of CMC regulatory and supply chain strategies for this novel production platform.

**3:00 Formulation and Manufacturing Considerations for Antibody-Drug Conjugates**
*Robert Henry Walters, Ph.D., Principal Scientist, Biotherapeutics Pharmaceutical R&D, Pfizer, Inc.*

This talk focuses on formulations of antibody-drug conjugates designed to ensure stability for a variety of conjugation chemistries and payload groups. Appropriate design of lyophilization cycles for antibody-drug conjugates will also be highlighted.

**3:30 End of Conference**

FINAL DAYS TO REGISTER



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# SPONSORSHIP & EXHIBITOR OPPORTUNITIES

CHI offers comprehensive packages that can be customized to your budget and objectives.

Sponsorship allows you to achieve your goals before, during, and long after the event. Packages may include presentations, exhibit space and branding, as well as the use of delegate lists. Signing on early will maximize your exposure to qualified decision-makers and drive traffic to your website in the coming months.

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

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

## INVITATION-ONLY VIP DINNER/HOSPITALITY SUITE

Select specific delegates from the pre-registration list to attend a private function at an upscale restaurant or a reception at the hotel. From extending the invitations, to venue suggestions, CHI will deliver your prospects and help you make the most of this invaluable opportunity.

## ONE-TO-ONE MEETINGS

Sponsors will select their top prospects from the conference preregistration list, and CHI will organize a guaranteed minimum number of face-to-face meetings.

## USER GROUP MEETING/CUSTOM EVENT

Co-locate your user group meeting or custom event. CHI will help market the event, manage logistical operations, develop the agenda, and more. CHI can handle the entirety of the meeting or select aspects.

## EXHIBIT

Exhibitors will enjoy facilitated networking opportunities with 1,200+ qualified delegates, making it the perfect platform to launch a new product, collect feedback, and generate new leads. Exhibit space sells out quickly, so reserve yours today.

**Additional branding & promotional opportunities include:**

- Conference Tote Bags
- Literature Distribution (Tote Bag Insert or Chair Drop)
- Badge Lanyards
- Program Guide Advertisement
- Padfolios and More...

**View Current Exhibitor List and Floor Plan**

**FOR ADDITIONAL INFORMATION, PLEASE CONTACT:**


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# HOTEL & TRAVEL INFORMATION

## Conference Venue and Hotel:

Westin Copley Place
10 Huntington Ave.
Boston, MA 02116
Phone: 617-262-9600

**Reservations:** Please visit the Travel page of BioprocessingSummit.com for further details and to book your hotel.

**Discounted Room Rate: $275 s/d**
**Discounted Cut-off Date: July 17, 2017**

## Top Reasons to Stay at the Westin Copley Place

- Complimentary Wireless Internet in your guest room
- Take advantage of the deeply discounted $275 group rate!
- Restaurants and shops are just minutes from the hotel
- Local attractions including Boston's South End, the Prudential Tower Skywalk and Boston Public Gardens within walking distance from hotel
- No Commute - conference takes place at the hotel

# 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 21, 2017.

- **Your research will be seen by leaders from top pharmaceutical, biotech, academic and government institutes**
- **Your poster abstract will be published in the conference materials**
- **Receive $50 off your registration fee**

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| Early Registration Deadline until June 16, 2017 | **$2845** | **$1455** |
| Advance Registration Deadline until July 21, 2017 | **$3045** | **$1555** |
| Registrations after July 21, 2017 and on-site | **$3245** | **$1625** |
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## How to Register: **BioprocessingSummit.com**

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**Please use keycode 1781F when registering**

### CONFERENCE DISCOUNTS

**Poster Submission - Discount ($50 Off):** Poster abstracts are due by July 21, 2017. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact jring@healthtech.com. *CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

**REGISTER 3 - 4th IS FREE:** Individuals must register for the same conference or conference combination and submit completed registration form together for discount to apply.

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If you are unable to attend but would like to purchase The Bioprocessing Summit CD for $750 (plus shipping), please visit BioprocessingSummit.com. Massachusetts delivery will include sales tax.

### ADDITIONAL REGISTRATION DETAILS

Each registration includes all conference sessions, posters and exhibits, food functions, and access to the conference proceedings link.

Handicapped Equal Access: In accordance with the ADA, Cambridge Healthtech Institute is pleased to arrange special accommodations for attendees with special needs. All requests for such assistance must be submitted in writing to CHI at least 30 days prior to the start of the meeting.

**To view our Substitutions/Cancellations Policy, go to www.healthtech.com/regdetails**

Video and or audio recording of any kind is prohibited onsite at all CHI events.