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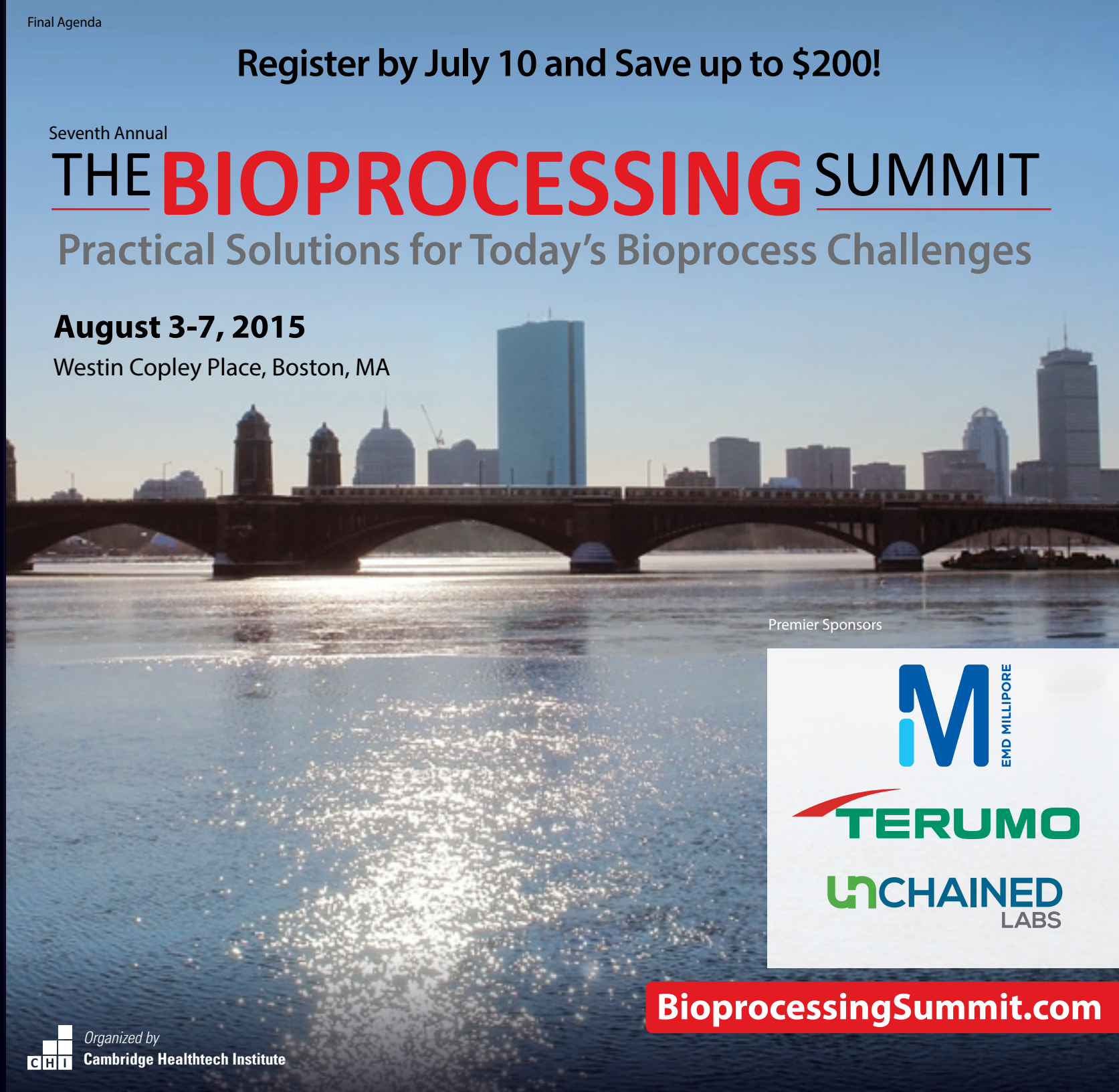

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About the Summit

The Bioprocessing Summit

The Bioprocessing Summit brings together international leaders from over 30 countries to discuss today's bioprocess issues, from cell line selection to manufacturing. The Summit provides practical details in a relaxed, congenial atmosphere that promotes information exchange and networking, and features Small-Group Breakout Discussions, a vibrant poster display, a busy Exhibit Hall, and networking Receptions. Spanning five days, the 2015 meeting includes 12 Conference Programs, 8 Training Seminars and 10 Short Courses.

Plenary Keynote Presentation:

4:45 pm, Wednesday, August 5

Meeting the Needs of Patients with Rare Diseases: Innovation in Product Development

Joanne T. Beck, Ph.D., Senior Vice President, Pharmaceutical Development, Shire Pharmaceuticals

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Event-at-a-Glance

	Monday - Tuesday August 3 - 4	Wednesday - Thursday AM August 5 - 6	Thursday PM - Friday August 6 - 7
STREAM #1 Cell Culture & Cell Line Development	Optimizing Cell Culture Technology	Bioproduction: Scale, Bioreactors & Disposables	Optimizing Cell Line Development
STREAM #2 Formulation & Downstream Processing	Overcoming Formulation Challenges for Biopharmaceutical Development & Manufacturing	High-Concentration Protein Formulations	Advances in Purification Technologies
STREAM #3 Analytical & Quality	Rapid Methods to Assess Quality & Stability of Biologics	Early Analytical Development for Biotherapeutics	Virus Detection, Clearance & Safety of Biologics
STREAM #4 Process Innovations & Cell Therapeutics	Cell Therapy Bioproduction	Continuous Processing in Biopharm Manufacturing	Advances in Purification Technologies
STREAM #5 Regulatory & Risk Management	Bioprocess Quality and Regulatory Compliance	Training Seminar: Current & Emerging Global Regulatory Expectations for Analytical Elements of Biotechnology/Biosimilar Products	Virus Detection, Clearance & Safety of Biologics
Cambridge Healthtech Training SEMINARS	**August 3-4** Day 1: 1:00-5:15pm Day 2: 8:30am-5:00pm	**August 5-6** Day 1: 9:00am-5:15pm Day 2: 8:30am-12:00pm	**August 6-7** Day 1: 2:00-5:30pm Day 2: 8:30am-4:30pm
	Introduction to Bioprocessing Introduction to Extractables & Leachables & Packaging	Introduction to Cell Culture Design of Experiments (DoE) for Bioprocess Analysis Current & Emerging Global Regulatory Expectations for Analytical Elements of Biotechnology/Biosimilar Products	Bulk API: Freeze-Thaw Operations Introduction to Lyophilization Introduction to Analytical Method Development & Validation for Therapeutic Proteins
	SHORT COURSES* **Monday, August 3** **9:00-11:30 am**	**DINNER SHORT COURSES*** **Tuesday, August 4** **6:00-8:30 pm**	**DINNER SHORT COURSES*** **Thursday, August 6** **6:30-9:00 pm**

**Separate registration required*

Short Courses*

MONDAY, AUGUST 3

Morning Short Courses | 9:00-11:30 am

SC1: Optimizing Media – Achieving Super Soup

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

Instructors:

David Brühlmann, MSc., Biotech Technology and Innovation, Biotech Process Sciences, Merck Serono SA

Michael Butler, Ph.D., Distinguished Professor, Microbiology, University of Manitoba

Kamal A. Rashid, Ph.D., Director, Biomanufacturing Education & Training Center, and Research Professor, Biology and Biotechnology, Worcester Polytechnic Institute

SC2: Biophysical Characterization in Assessing the Higher Order Structure (HOS) Fingerprint of Biopharmaceuticals

In this short course, we will focus our attention on discussions concerning the integral role that biophysical characterization plays in assessing the higher-order structure (HOS) of biopharmaceuticals. The development this fingerprint is a key element in assessing information on the HOS of these biopharmaceuticals, which is then employed as the master comparator for evaluating the developability properties of these molecules (in drug candidate selection studies), in assessing their stability (in formulation selection) and in establishing comparability (in terms of drug variant analysis, final product consistency and in assessing the impact of manufacturing changes). A large part of this course will explore the development of this fingerprint using three approaches: low-resolution biophysical characterization, assessing biophysical properties, and advanced high-resolution biophysical characterization.

Instructor:

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

SC3: Accelerated Stability Testing of Biologics

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

Instructor:

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

TUESDAY, AUGUST 4

Dinner Short Courses | 6:00-8:30 pm

SC4: Analytical Strategies for Comparability in Bioprocess Development

Bioprocess changes can impact quality attributes of biologics and may affect efficacy and/or safety of the product. During development and throughout the product lifecyle, when process improvements are implemented, it is essential to gather sufficient data to support the conclusion that product safety or efficacy has not been adversely affected. This demonstration exercise requires careful planning of the comparability studies and is based on the background knowledge of protein structure, biological function, and clinical attribute profiles of the product accumulated during development. In this short course, we will discuss the key concepts of defining critical product quality attributes, the common analytical characterization technologies used, considerations in process monitoring and controls, and the iterative process of demonstrating comparability of the product in support of process changes.

Instructor:

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

SC5: Operational Excellence Strategies for Bioprocessing – QbD, DoE and PAT

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

Instructor:

Elizabeth Rebeil, Associate Director, Operational Excellence, Shire Pharmaceuticals

SC6: Protein Aggregation: Mechanism, Characterization and Consequences

Protein aggregation is recognized by regulatory agencies and the biopharmaceutical industry as a key quality attribute of biotherapeutic products. Various aggregates hold the potential for adversely impacting production and patients in a variety of ways. This in-depth workshop reviews the origins and consequences of aggregation in biotherapeutics, and then examines strategies for predicting and quantifying aggregation in biopharmaceuticals. It benefits scientists engaged in development, production, analytical characterization and approval of biotherapeutics and who require a good working knowledge of protein aggregation.

Instructor:

Thomas Laue, Ph.D., Professor, Biochemistry and Molecular Biology; Director, Biomolecular Interaction Technologies Center (BITC), University of New Hampshire

David F. Nicoli, Ph.D., Vice President, R&D, Particle Sizing Systems, LLC

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

Short Courses*

Tuesday, August 4 Dinner Short Courses (Cont.)

SC7: Patent Strategies for Bioprocess Scientists

While the adage "the product is the process" may overly stress the influence of production processes on a biologic's attributes, there is clearly a strong relationship between the manufacturing process for making a biologic and the biologic's final characteristics. The growth of biosimilars is leading many to seek second-generation patents, particularly for bioproduction, prompting legal moves to help protect trade secrets and give more freedom to operate. The ability to recognize and take advantage of follow on intellectual property can be invaluable to a products commercial success.
Instructor:
Paul Calvo, Ph.D., Director, Biotechnology/Chemical Group, Sterne, Kessler, Goldstein & Fox

SC8: Incorporating the Concepts of Pharmaceutical Quality Systems into Cell Therapy Products

This short course is designed to provide a concise examination of current quality system issues affecting the manufacturers of cell based biological products. The topics of this course will touch upon; Good Manufacturing Practice (GMP) compliance and auditing, Good Documentation Practices, Quality system management, Quality risk management and tools, Microbiology and Contamination Control, Process Analytical Technology (PAT) implementation and Quality by Design (QbD), Out of Specification (OOS) investigations and CAPA systems. The course provides an opportunity to improve business and technical knowledge in the area of quality systems, leadership traits to succeed, as well as communication and regulatory process skills. Course attendees will be better prepared to appreciate, improve and update the quality systems necessary to succeed in the regulatory approval process.
Instructor:
Gary du Moulin, Ph.D., M.P.H., RAC, Adjunct Associate Professor, Massachusetts College of Pharmacy & Health Sciences

THURSDAY, AUGUST 6

Dinner Short Courses | 6:30-9:00 pm

SC9: Transient Protein Production in Mammalian Cells

This short course introduces both the fundamental concepts and technologies needed to establish transient protein production in mammalian cells. This allows for the rapid generation, purification and characterization of milligram-to-gram quantities of secreted or intracellular recombinant proteins for therapeutic, functional and structural studies. The course combines instruction and case studies in an interactive environment.
Instructors:
Richard Altman, MS, Research Scientist, Molecular Sciences, Alexion Pharmaceuticals
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, Leidos Biomedical Research, Inc.

SC10: ABC: Anything But Chromatography – Precipitation, Crystallization and Flocculation

The process developed for manufacturing of biopharmaceuticals has a strong new focus. Strategies for economical processing due to increased titer became very important. Precipitation, crystallization and flocculation are unit operations which overcome productivity limits of chromatography and they are linear scalable. Principles on how to set up a precipitation, crystallization, or flocculation process for purification of recombinant proteins will be given. Reactor configurations and scale up rules will be explained. Full length antibodies, single chain antibodies and cytokines will be used as examples and strategies how to implement such processes will be discussed.
Instructor:
Alois Jungbauer, Ph.D., Professor, Department of Biotechnology, University of Natural Resources and Life Science Vienna, (BOKU) and Austrian Centre of Industrial Biotechnology (acib)

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

Cambridge Healthtech
Training SEMINARS

AUGUST 3-4, 2015
DAY 1 1:00-5:15 PM • DAY 2 8:30 AM-5:00 PM

(TS1) Introduction to Bioprocessing

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

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

CHI's Introduction to Bioprocessing training seminar offers a comprehensive survey of the steps needed to produce today's complex biopharmaceuticals, from early development through commercial manufacturing. The seminar begins with a brief introduction to biologic drugs and the aspects of protein science that drive the intricate progression of analytical and process steps that follows. We then step through the stages of bioprocessing, beginning with the development of cell lines and ending at scaling up for commercial production. The seminar also explores emerging process technologies, facility design considerations and the regulatory and quality standards that govern our industry throughout development. The important roles of analytical methods at all stages of development as well as formulation and stability assessments in developing and gaining approval for a biopharmaceutical are also examined. This 1.5-day class is directed to attendees working in any aspect of industry, including scientific, technical, business, marketing or support functions, who would benefit from a detailed overview of this field.

Instructor Biographies:

Frank J Riske, Ph.D., Senior Consultant at BioProcess Technology Consultants has over 25 years of experience in the biopharmaceutical industry. Prior to joining BioProcess Technology Consultants, Dr. Riske was Senior Director in the Late Phase Process Development Group at Genzyme, a Sanofi company. Before Genzyme, Dr. Riske held positions at Epic Therapeutics, Repligen and Hoffmann-LaRoche. Dr. Riske has extensive experience in the development of downstream processes for cytokines, proteins and virus from plasma, E coli, Pichia and mammalian systems and in the development and manufacture of novel drug delivery systems. Dr. Riske received his B.S. in Biology from Fairfield University, Ph.D. in Biochemistry and Microbiology from Rutgers University and completed a post-doctoral position at Hoffmann-LaRoche.

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

(TS2) Introduction to Extractables and Leachables and Packaging

Diane Paskiet, MS, Director of Scientific Affairs, West Pharmaceuticals

Chemical substances can be leached into biologics from various components used in the manufacture, storage or delivery of a therapeutic product leading to a negative impact on the product and potential for an undesirable effect on the patient. This 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. Over the 1.5 days the following topics will be addressed.

Instructor Biography:

Ms. Paskiet has over twenty years of experience in polymer analysis relating to product failures, deformulation and migration studies. She has served as a project advisor in support of qualification studies associated with container closure systems for IND and NDA filings. Her current responsibilities include coordination of studies for technical support and R&D. Previous to this role she was in charge of site operations for West-Monarch Analytical Laboratories.

AUGUST 5-6, 2015
DAY 1 9:00-5:15 PM • DAY 2 8:30 AM-12:00 PM

(TS3) Introduction to Cell Culture

Timothy W. Fawcett, Ph.D., Director, The BioTechnical Institute of Maryland, Inc.; Founder, BioSciConcepts

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

Instructor Biography:

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

Cambridge Healthtech
Training SEMINARS

(TS4) Design of Experiments for Bioprocess Analysis

Marcello Fidaleo, Ph.D., Teaching Fellow at the Biomanufacturing Training and Education Center (Raleigh, NC, USA); Assistant Professor at University of Tuscia (Viterbo, Italy).

The aim of this training seminar is to provide the attendees with an introduction to the Design of Experiments (DoE) methods applied to analysis and optimization of bioprocesses. The seminar focuses on the practical application of DoE methods through the use of lectures, JMP statistical software (SAS Institute, NC) and bioprocess case studies. The case studies, which provide real data, focus on protein production by microbial fermentation, chromatography and pharmaceutical product formulation. Attendees will receive a practical overview of the following topics: basic statistical concepts required for DoE, how to use factorial, fractional factorial, and response surface designs for the characterization and optimization of bioprocesses, and how to interpret the output of experimental design software (normal probability, interaction, contour and residual analysis plots or estimated coefficients tables for factorial or surface response models). The course is targeted to all those interested in bioprocess development and optimization.

Instructor Biography:

Marcello Fidaleo is an assistant professor at the University of Tuscia, Italy, where he teaches unit operations and design and analysis of experiments for the food and biotechnology industry. He has more than ten years of experience in design of experiments and data modeling in the field of membrane separation, enzymatic and microbial processes in the area of food, chemistry and biotechnology. Dr. Fidaleo holds a master's degree in Chemical Engineering from the Sapienza University of Rome and a doctorate in Food Biotechnology from the University of Tuscia.

(TS5) Current and Emerging Global Regulatory Expectations for Analytical Elements of Biotechnology/Biosimilar Products

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

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

Instructor Biography:

Nadine Ritter obtained her master and doctoral degrees in cell and molecular biology at Rice University (Houston, TX) on evolutionary mechanisms for subcellular translocation of mitochondrial proteins. She was engaged in basic academic research in the field of extracellular matrix proteins and the process of bone mineralization at the University of Texas Health Science Center in Houston for over 10 yrs. She entered the biopharm industry as a protein chemist in analytical R&D at Abbott Laboratories (Abbott Park, IL). She then became the Director of the Analytical Services Division of BioReliance (Rockville, MD), a major contract testing organization. There, she led a team of CMC scientists in the design and conduct of method qualification, validation, and transfer, product characterization and comparability studies, and QC release and stability testing. She managed quality and compliance activities for the R&D, GLP and GMP activities conducted in her lab, and implemented Part 11 computer system requirements. In 1999, she created the first public training course specifically focused on biotechnology stability programs, which later grew into an award-winning CMC analytical training course. Since 2002 she has been an international consultant, trainer, speaker and writer for biotech and biosimilar products. In 2003, she was one of six industry and two FDA founders of the CaSSS CMC Strategy Forum, which has led to the publication of major industry/regulatory white papers on CMC topics, and is now being held annually in North America, Europe, Asia and Latin America.Since 2002, she has been an international consultant, trainer, speaker and writer for biotech and biosimilar products. She first worked independently as NMR Biotech Services (Germantown, MD), then in 2004 joined Biologics Consulting Group, Inc. (Alexandria, VA). In 2014, she decided to return to independent consulting, forming Global Biotech Experts, LLC.

AUGUST 6-7, 2015
DAY 1 2:00-5:30 PM • DAY 2 8:30 AM - 4:30 PM

(TS6) Bulk API: Freeze-Thaw Operations

Parviz A. Shamlou, Ph.D., George B. and Joy Rathmann Professor, and Director, Amgen Bioprocessing Center, Keck Graduate Institute

Freeze-thaw is a key unit operation in biomanufacturing, but despite its wide spread use, it is treated more as activity than a unit operation. In this seminar a new method of freeze–thaw is described using experimental data obtained from freezing of purified API solution including proteins and monoclonal antibodies. The method is based on freezing protein solutions in rectangular rather than cylindrical containers. It is hypothesized that the change in container geometry allows for linear scale-up of the freeze–thaw operation based on equivalency of temperature–time profile. The hypothesis is tested using freeze–thaw data from a miniature (30 ml) and a 2.4 litre container. Computational fluid dynamics techniques are used to simulate the freeze process and the simulations are compared with experimental results. Protein quality is assessed as a function of freeze conditions using dynamic light scattering, circular CD, size-exclusion and reverse-phase HPLC measurements. The results demonstrate the applicability of the new approach. Freezing of protein solution at concentrations of approx. 200 mg/ml is shown to be possible with no damage to the molecule for multiple cycles of freeze–thaw. The results are scaled-up and confirmed using data from full-scale operation in a biomanufacturing setting.

Target Audience:

Scientists and engineers working in different functional areas in API and Drug Product (DP) including Bioprocess Design and Development (BR&D), Analytical and Biophysical Characterization and Drug Product Formulation.

What students will gain from attending the seminar:

Students attending the seminar will learn how to combine and use basic knowledge of heat transfer, scale-down, first principle modeling, DOE and QBD to design unit operations for freezing and thawing of bulk API in a biomanufacturing setting.

Instructor Biography:

Dr. Shamlou is chemical engineer with over 30 years of academic and industry experience bioprocess design and development with emphasis on biopharmaceutical therapeutics

Dr. Shamlou received his first academic appointment in 1983 in the Department of Chemical and Biochemical Engineering at University College London (UCL). At UCL, Dr. Shamlou pioneered new areas of bioprocessing research at the interface with life

science discoveries, with an emphasis on the creation of new scale-down methods and miniaturization to speed up the translation of discovery to outcome, and to allow prediction of full-scale bioprocessing of advanced biologics, including therapeutic genes, antibodies and cellular systems. This work included biophysical characterization of non-viral drug delivery systems, the design of miniaturized techniques for fermentation and cell-culturing operations and the bioprocess engineering issues related to manufacturing of advanced vaccines and tissue-engineered products. His research at UCL was supported by 20 different industry and government grants and 35 PhD and postdoctoral researchers.

In 2003 Dr. Shamlou joined Eli Lilly and Company's headquarters in Indianapolis, Indiana where he was responsible for innovation and technology evaluation for development and commercialization of biotherapeutics. At Eli Lilly and Company Dr. Shamlou extended his first principle approaches combined with scale-down techniques to improve manufacturing operations of registered products and speed up development of pipeline molecules from discovery to commercialization. Projects worked on included insulin, human growth hormone and several monoclonal antibody molecules currently in development for treatment of Alzheimer's, rheumatoid arthritis, cancers, diabetes and lupus.

During his 30 years of industry and academic work Dr. Shamlou also served on several scientific committees and boards including European Federation of Biotechnology and UK's Institution of Chemical Engineers (IChemE). Dr. Shamlou was the Editor-in-Chief of the peer-reviewed Journal of Biotechnology and Applied Biochemistry (2003-2012). He is a Fellow of the British Institution of Chemical Engineers. He is the co-author of over 200 publications in peer-reviewed journals, chapters in books and presentations at national and international conferences and reports.

(TS7) Introduction to Lyophilization: Theory and Practices

Edward H. Trappler, President, Lyophilization Technology, Inc.

Discussions of the basic principles covering the theories and practices provide an introduction to those entering the field as well as an update to experienced scientists. This seminar is geared to those developing new products, involved in technical services and technology transfer, overseeing manufacturing, and responsible for quality control. Considerations for stabilizing bulk drug substances as well as preservation of finished drug product will be presented. Starting with a process overview, subsequent focus will be on each process step, with correlation to CPP and CQA. Included in the discussions will be finished product qualities and well as considerations during development and technology transfer in preparation for commercial manufacturing.

Instructor Biography:
Ed Trappler has dedicated his professional career to the study, implementation and advancement of the science and technology of lyophilization. In 1992, he founded Lyophilization Technology, Inc. to continue his aspiration of establishing a source of scientific and technical services while expanding the knowledge and understanding of lyophilization within the industry. He is actively involved in Business Development, the Scientific Advisory Board, and Marketing.Instructor. Mr. Trappler has over 35 years' experience in lyophilization that ranges from product development to equipment application engineering. His experience in the pharmaceutical industry includes product development, toxicology supply preparation, clinical manufacturing, and parenteral production. Prior to founding the company, he served as a Systems Application Engineer for Hull Corporation. Mr. Trappler received his Bachelor of Science degree in Chemistry from The College of New Jersey. Active in promoting lyophilization in the health care industry, Mr. Trappler has contributed chapters to six books, and authored and presented numerous papers and courses in freeze drying across the North American, European and Asian continents. He has received numerous recognitions for contributions to the industry. He is an active member of the PDA, serving on a number of committees, including as chairperson of the Lyophilization Interest Group and Validation Task Force. The PDA awarded him the Gordon Personeous award for his long term contributions to the PDA and the James Agalloco award for his contribution to education. He is also a member of the AIChE, and has been active in and presents for the AAPS, ISPE, and ISL-FD.

(TS8) Introduction to Analytical Method Development and Validation for Therapeutic Proteins

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

This course is a panoramic review of analytical method development and validation for therapeutic proteins, including antibodies and enzymes. It is intended for scientists working on therapeutic proteins in Analytical Development, Quality Control, Product Development or related functional areas. It starts with basic knowledge of work on therapeutic proteins: manufacturing of proteins 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 Biography:
Dr. Jichao Kang holds a Ph.D. in Pharmaceutics and has been working on characterization, method development and validation and formulation for protein therapeutics since 1995. He is an accomplished researcher with over 15 peer-reviewed journal articles and book chapters, several patents and numerous conference presentations. The proteins he has worked on extensively include cytokines, antibodies, enzymes and protein conjugates. He is a key contributor in dozens of IND/IMPD and BLA/MAA filings. He is currently the Director of Analytical and Formulation Development at Gallus BioPharmaceuticals NJ, LLC, one of the leading CMOs for biologics, and held the same position at Laureate BioPharma before it was acquired by Gallus. Prior to Laureate, he was the department head of Analytical Development at Auxilium Pharmaceuticals, Inc., and was a key contributor in Auxilium's successful marketing application of Xiaflex in both U.S. and EU. He also worked in MedImmune, PDL, and Neose Technologies.

To view Training Seminar Agendas in full, visit:
BioprocessingSummit.com/BPD/Training-Seminars

Optimizing Cell Culture Technology

Enhancing Knowledge for Growing Cells

MONDAY, AUGUST 3

8:00 am Pre-Conference Registration and Morning Coffee

9:00-11:30 Recommended Short Course*
Optimizing Media - Achieving Super Soup
* Separate registration required; click here for details.

11:30 Main Conference Registration

CULTURING CHO CELLS

1:00 pm Chairperson's Opening Remarks
Tiffany Rau, Ph.D., Global Technical and Technology Manager, Eli Lilly and Company

» 1:10 OPENING KEYNOTE PRESENTATION:
Getting to the Root of the Problem: What are the Fundamental Factors Limiting Growth and Productivity in CHO Cell Cultures?
Gregory Hiller, Ph.D., Associate Research Fellow, Culture Process Development, BioProcess R&D, Pfizer, Inc.
Why do they stop growing?!? We will describe experimental strategies undertaken over the last eight years in my group to answer this most basic question and understand the underlying cellular metabolism. We will also explain our methods of overcoming the problem of growth cessation of CHO cells which have enabled dramatic increases in overall culture productivity in the industry standard fed-batch culture and in less common modes of bioreactor operation.

1:45 Development and Manufacturability Assessment of Chemically-Defined Medium for the Production of Protein Therapeutics in CHO Cells
Wai Lam W. Ling, Ph.D., Senior Principal Scientist, Process Development & Engineering, Biologics BioProcess Development, Merck Research Labs
Internally developed chemically-defined (CD) media offers flexibility for protein production process development. Through DOE screenings and component optimization, a CD basal medium (CDM) was developed for CHO cell culture. Culture performance of CDM manufactured by vendors was poor compared to in-house preparation. An investigation revealed key medium components were sensitive to commercial manufacture. CDM was subsequently reformulated into a manufacture-compatible core medium with sensitive components supplemented separately.

2:15 Host Cell Protein Expression during Extended CHO Cell Culture
Kristin Valente, Ph.D., Associate Principal Scientist, Merck
As the biopharmaceutical industry moves towards continuous bioprocessing, it is important to consider the impact of extended CHO culture on extracellular HCP expression, particularly for impurities that are difficult to remove during purification. Proteomic techniques were applied to evaluate HCP expression over 500 days of culture. The effect of cell age on the HCP impurity profile is presented and implications of variable HCP expression on downstream purification are discussed.

2:45 Refreshment Break

ANALYSIS APPROACHES & AMBR

3:15 Optimizing Cell Culture Processes and Associated Analytical Methods
Lada Laenen, Ph.D., Senior Director, Manufacturing Science and Technologies, Genzyme

3:45 Enhanced Process Consistency, Robustness and Success in Cell Line Selection Using High-Throughput Bioreactors
Wenqi Xie, Associate Scientist II, Cell Culture Development, Biogen Idec, Inc.
AMBR is now a common high-throughput bioreactor option for process development and cell line selections. At Biogen, we evaluated the robustness of our platform process in AMBR and determined important levers that affect cell culture performance and product quality attributes. Moreover, through systematic retrospective and prospective evaluations of cell line screening results from multiple projects, we proposed the optimal number of cell lines to screen and therefore recommend using high-throughput bioreactors to achieve target titer in cell line selections.

4:15 Breakout Discussions
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. Then continue the discussion as you head into the lively exhibit hall for information about the latest technologies.

5:15 Discussion Report-Outs

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

7:00 End of Day

TUESDAY, AUGUST 4

7:30 am Registration and Morning Coffee

OPTIMIZING PROCESS DEVELOPMENT

7:55 Chairperson's Remarks
Martin Heitmann, Ph.D., Senior Scientist, Cell Culture Technology, Novo Nordisk A/S

» 8:00 FEATURED PRESENTATION:
Delivering the Pipeline: A Global Perspective of Process Development and Design for Manufacturing
Tiffany Rau, Ph.D., Global Technical and Technology Manager, Eli Lilly and Company

8:30 Prediction of Cell Culture Performance and Molecule Quality Attributes from Micro-Scale Fed-Batch Cultures
CASE STUDY *David Brühlmann, MSc., Biotech Technology and Innovation, Biotech Process Sciences, Merck Serono SA*
The selection of a fed-batch cultivation system is often based on throughput and cost. However, the process

Optimizing Cell Culture Technology

Enhancing Knowledge for Growing Cells

knowledge derived from different systems and scales is not necessarily identical. Hence, a careful evaluation of systems which are already established or newly implemented is essential. Here, we describe the performance of 12 different recombinant CHO cell lines expressing the same antibody in fed-batch culture systems ranging from a few hundred microliters to lab scale. The 12 cell lines were selected based on distinct phenotypes covering a range which can be expected in typical industrial process development projects. The cell lines were cultivated using the same expansion and fed-batch protocol. The following cultivation systems were evaluated: shaking 96-deepwell plates, 50 mL vented shake tubes, micro- and lab-scale bioreactors. The results of this study show both the limitations and the potential of each cultivation system, their suitability for process development, process characterization and scale-up.

9:00 Novel Virus-Like Particle and Nanoparticle Vaccine Production – An Overview of Cell Culture Process Development

Payal Biswas, Ph.D., Scientist, Upstream Process Development, Vaccine Production Program, Vaccine Research Center/NIAID/NIH

In order to rapidly produce novel VLP vaccines and nanoparticle influenza vaccines for Phase I clinical trials, a mammalian cell culture-based, robust transient transfection platform process was developed. Transfection conditions and process parameters were optimized to achieve a viable yield for clinical production and scaled up to 50L fully disposable bioreactor system for GMP manufacturing. Background and supporting data for Phase I manufacturing of these vaccines will be presented.

9:30 Manufacturing Core Competency for Biosimilar Contenders

Sponsored by JSB 健顺生物 IOSCIENCES

Shun Luo, Ph.D., CEO & President, Jianshun Biosciences Co., Ltd.

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

METABOLIC FLUX ANALYSIS & QUALITY

10:30 Applications of Metabolic Flux Analysis to Process Development

Neil Templeton, Ph.D., Senior Scientist, Bioprocess Development, Merck Research Laboratories

11:00 Towards Cell Engineering Using ^{13}C-Metabolic Flux Analysis and Insight from Cancer Metabolism

Woo Suk Ahn, Ph.D., Postdoctoral Associate, Chemical Engineering, Massachusetts Institute of Technology

Cancer metabolism is a promising topic to be utilized for cell engineering field. Cancer cells quickly produce bioenergy and anabolic precursors by aerobic glycolysis that is increased significantly under hypoxia. Here, we quantified cancer metabolism using ^{13}C-metabolic flux analysis and validated by gene knock-down/overexpression techniques. We revealed how rapidly growing cells coordinate metabolism to survive and proliferate under hypoxic condition.

11:30 5-Hydroxymethylcytosine (5hmC) Barcoding and Cell Identity

Richard R. Meehan, Ph.D., Project Leader, Chromosomes and Gene Expresion, MRC Human Genetics Unit, IGMM, University of Edinburgh

An assumption underlying the use of cultured cells is that they retain and mimic the molecular characteristics of the tissue from which they were derived or conform to an industry standard that enables their reproducible use in bio-manufacturing. By studying the establishment of fibroblasts and T-cells in culture, we found that adaptation resulted in a rapid and comprehensive re-programming of the transcriptome and epigenome, indicative of an altered cell state. Re-programming involved almost complete loss of 5hmC in cultured cells. Restoration of 5hmC profiles is indicative of restoration of cell identity.

12:00 pm From Upstream to Downstream: Large-Scale, High Titer Transient Transfection Platform for Biomanufacturing

Sponsored by MaxCyte

James Brady, Ph.D., Vice President, Technical Applications and Customer Service, MaxCyte

Harmonizing upstream and downstream processes can reduce the time it takes to move a biotherapeutic to market. In this presentation, data developed with MaxCyte's flow electroporation, closed, single-use, cGMP-compliant system will demonstrate large-scale transient transfection in CHO cells and biologically relevant cells and the resulting high titers. The results demonstrate the platform's scalability, high transfection efficiency, and cell viability. The outcome is a cost-efficient, timely high yield and a harmonization between upstream and downstream.

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

1:15 Session Break

PERFUSION PRODUCTION

1:55 Chairperson's Remarks

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

2:00 Scale-Down Tools for Evaluation of Perfusion Cultivations

CASE STUDY UNPUBLISHED DATA

Martin Heitmann, Ph.D., Senior Scientist, Cell Culture Technology, Novo Nordisk A/S

Strategies are presented to enable screening of multiple process parameters at different scales, while being focused on simple, yet predictive, scale down models for perfusion processes. Due to the difficulty of implementing cell retention in small scale, a chemostat based scale-down system was developed. The conception of a repeated exponential fed-batch scheme to mimic chemostat cultivations is described and its implementation in 10 mL scale ambrTM system cultures is presented. This system is then compared to classical bench top chemostat and ATF perfusion cultures.

2:30 Progress towards Efficient Implementation of Continuous Upstream Processes in Early Development

CASE STUDY UNPUBLISHED DATA

Daryl Powers, Ph.D., Senior Scientist, Early Cell Culture Development, Sanofi Global Biotherapeutics

We have implemented several strategies to streamline early process development for perfusion

production of a therapeutic IgG that is being readied for transfer to the pilot plant for clinical material generation. These strategies include some perfusion-specific techniques in addition to many of the same tools and methods that are used for fed-batch process development.

3:00 Optimizing Osmolality and Cell Expansion Strategy to Improve Cell Culture Performance in a Perfusion-Based Bioreactor Process

CASE STUDY UNPUBLISHED DATA *Christopher Rives, Ph.D., Senior Upstream Development Engineer, BioProcess Development, Shire plc*

During development of a perfusion-based bioreactor process for production of a therapeutic protein, a significant amount of variability in bioreactor terminal viable cell density and viability profiles was observed. This presentation describes the approaches taken to investigate the potential root causes of performance variability and summarizes the key experimental findings. In addition, the proposed control strategy will be shared.

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

TOOLS AND TECHNOLOGIES TO ENHANCE CELL CULTURE PROCESSES

4:15 Biologics Data Platform for Tailored Support of Cell Line Development

Christian Bender, Ph.D., Computational Biologist, Global Drug Discovery, Global Biologics, Bayer HealthCare

We have successfully implemented the Biologics Data Platform (BDP) for tailored support of our screening and protein production processes. In the context of our cell line development process, we present the integration of BDP with our automation workstation. We demonstrate the power of using a comprehensive data management platform to track data for cell line clones and fed-batch experiments together with molecule information such as primary sequences and experimental results.

4:45 Portable X-Ray Fluorescence Spectrometer: A Tool for Biopharmaceutical Forensic Investigations

Jessica Mondia, Ph.D., Research Scientist, Biogen Idec, Inc.

A portable X-ray fluorescence (XRF) spectrometer is a small, cheap, easy and fast instrument for multi-elemental analysis. In biopharma, forensic investigations usually refer to determining the root-cause and evaluating the risks associated with deviations from GMP guidelines including batch records, procedures and SOPs. Here we introduce the use of a XRF spectrometer for biopharmaceutical forensic applications as an in-house-portable diagnostic tool to help resolve or guide investigations in a timely fashion.

5:15 Close of Conference

6:00-8:30 Recommended Dinner Short Course*
Operational Excellence Strategies for Bioprocessing – QbD, DoE and PAT

* Separate registration required; click **here** for details.

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The **Intro-Net** offers you the opportunity to set up meetings with selected attendees before, during and after this conference, allowing you to connect to the key people you want to meet. This online system was designed with your privacy in mind and is only available to registered session attendees of this event.

Bioproduction: Scale, Bioreactors & Disposables

Making It Work

WEDNESDAY, AUGUST 5

7:00 am Registration and Morning Coffee

OPTIMIZING PROCESSES FOR GREATER PRODUCTIVITY

8:05 Chairperson's Remarks

Eric J. Wallenstein, Ph.D., Associate Principal Scientist, Biologics Manufacturing Science & Commercialization, Merck & Co., Inc.

» 8:15 OPENING KEYNOTE PRESENTATION:

Planning for the Future: Manufacturing Capacity Versus Demand Uncertainty

Peter F. Moesta, Ph.D., Senior Vice President, Biologics Development & Operations, Bristol Myers Squibb Co.

The rapid advancements in Immuno-Oncology at BMS have created a unique challenge for Development and Manufacturing. In-licensed molecules that were in early development are being accelerated and putting pressure on commercial process development and readiness. Commercial capacity needs to be made available although neither dose nor volumes are defined. The talk will describe the strategy that is being used combining capabilities in process development, capacity expansions, and leveraging a network of CMOs to address both the potential and the risks of a rapidly developing portfolio of new life-saving drugs.

9:00 Fc-Fusions Versus mABs: Opportunities and Limits of Platform Processes

Stefan Schmidt, Ph.D., MBA, Vice President, Process Science & Production, Rentschler Biotechnologie GmbH

In theory, Fc-fusion proteins should behave quite comparably to mABs, both in upstream and downstream processes. However, in practice some differences can be observed. Well-established platform processes only rarely and partially match the requirements for Fc-fusion proteins. I will discuss the range of manufacturing possibilities for fusion proteins with regard to platform processes, modular concepts, and fully customized solutions in comparison to conventional antibody production.

9:30 Challenges in N-1 Perfusion Process Optimization

UNPUBLISHED DATA *Weimin Lin, M.D., Process Development Scientist, Biogen Idec, Inc.*

Implementing an N-1 perfusion process at large-scale manufacturing can increase capacity and lower manufacturing costs at Biogen Idec. Perfusion N-1 enables high-seed fed-batch production, which can increase manufacturing capacity by increasing volumetric productivity. However, there are significant challenges in N-1 perfusion process development, such as identifying the proper equipment, improving media formulations, developing a platform process, and scaling-up to the manufacturing facility. This talk will focus on media aspects relating to the above challenges.

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

10:45 A Risk-Based Strategy for Implementing Disposables in a Commercial Manufacturing Process

Chad Atwell, M.S., Associate Director, Manufacturing Science and Technology, Genzyme Corporation

A risk assessment strategy is used to plan the implementation of disposables in a commercial protein purification process. The results influence extractable and leachable study design as well as a dual vendor sourcing strategy to ensure business continuity. An overview of the implementation program is reviewed.

11:15 Effects of Antifoam on High Density Perfusion Cultures: A Case Study Using Small Scale Models

CASE STUDY *Jonathan Wang, Process Engineer Associate, Late Stage Cell Culture Development, Sanofi*

11:45 A High-Yield Single-Use System for Biosimilar Process Development Using Eppendorf Bio-BLU® Single-Use Vessels and the BioFlo® 320 Bioprocess Control Station

Sponsored by eppendorf

Stacey Willard, Ph.D., Senior Research Scientist, Applications R&D Lab, Eppendorf

12:00 pm Increasing Protein Production with Novel Cell Ess Supplement without Affecting Metabolic Profile

Sponsored by essential pharmaceuticals, LLC

Adam Elhofy, Ph.D., CSO, Essential Pharmaceuticals

Enhancing protein production is a common goal in the biomanufacturing industry. At a concentration of 1% Cell Ess supplement resulted in a 37% increase in productivity. When using the supplement as a feed it resulted in in a 25% increase in yield and an extension of peak protein production. Our results suggest that an increase in protein production may not necessarily require a change in the metabolic state of the cells.

12:30 Luncheon Presentation: Ensuring Scalable Performance of Single-Use Bioreactors from Bench to Clinical Scale

Sponsored by EMD Millipore

Janice Lloyd Simler, Ph.D., Global Senior Product Manager, EMD Millipore Corporation

Bioreactor process set points and parameters developed in bench-top bioreactors are used in the large production scale bioreactors. It is therefore crucial that the set points developed at the small scale can be easily transferred to large scale. This presentation will highlight how a detailed understanding of the performance design space of each sized bioreactor can enable the selection of process parameters at each scale that will enable scalable performance across the platform.

1:30 Session Break

SCALING DOWN

1:55 Chairperson's Remarks

David Kolwyck, MBA, Director, Manufacturing Sciences, Raw Materials, Biogen Idec, Inc.

2:00 Scale-Down Models for Technology Transfer and Process Characterization of an Upstream Cell Culture Process

CASE STUDY *Eric J. Wallenstein, Ph.D., Associate Principal Scientist, Global Vaccines & Biologics Commercialization, Merck & Co., Inc.*

Bioproduction: Scale, Bioreactors & Disposables

Making It Work

2:30 Overcoming Scale-Down Model Development Challenges for MAb Production

CASE STUDY *Stephen Hsu, MSc., Senior Research Associate II, Gilead Sciences*

A case study is presented that highlights the challenges encountered with a sensitive CHO cell line expressing a therapeutic monoclonal antibody (mAb) that exhibited reduced productivity upon scale translation. Various scale-down model strategies were leveraged to assess the scalability issues and identify several raw materials and process parameters that led to the reduced titer. Process enhancements were made, based on the scale-down models, to enable subsequent successful large-scale production runs.

3:00 Small-Scale Model Development & Application for a Commercial Legacy Process

CASE STUDY UNPUBLISHED DATA *Hunter Malanson, Scientist I, Upstream Development, Alexion Pharmaceuticals*

Significant disparities in scale between commercial production and laboratory bench bioreactors were observed for a legacy process. A qualified 5L small scale model was iteratively developed to mimic the commercial production bioreactor's behavior and metabolic profile. Cell growth, viability, and productivity trends were closely matched while product quality attributes were maintained. This model is now being actively applied for potential changes and process knowledge for this late-stage commercial process.

3:30 Rapid Development of an Inclusion Body Production Process in *E. coli* Using Automated Mini-Bioreactor System

CASE STUDY *Matthew Manahan, Scientist, Bioprocess Development, Merck & Co., Inc.*

This work highlights development of an inclusion body fermentation process using the automated mini-bioreactor system (ambr250TM). With this HTPD approach we were able to screen multiple expression plasmids, seven sequence variants, and process parameters to achieve 50% improvement in fermentation productivity with comparable protein purity over the platform approach. The process development is achieved within 4 months with total of 120 batches, before being successfully scaled up to 30-L.

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

PLENARY SESSION

4:45 Chairperson's Remarks

Sam Ellis, Vice President, Biochemist, Thomson Instrument Co.

» **4:50 PLENARY KEYNOTE PRESENTATION:**
Meeting the Needs of Patients with Rare Diseases: Innovation in Product Development

Joanne T. Beck, Ph.D., Senior Vice President, Pharmaceutical Development, Shire Pharmaceuticals

At Shire, where the delivery of innovative medicines to patients with rare diseases and other specialty conditions is a fundamental component of the business model, creative solutions are critical to our success. Starting with the transition of drug candidates from discovery research to the clinic, followed by late phase development and eventually commercial product lifecycle management, scientists and engineers focus on both technology innovation and creative business approaches to deliver high quality therapies to the patients while decreasing development timelines and costs.

5:20 Interactive Panel Discussion: How to Innovate Product Development

- Technologies
- Strategies
- Cutting Costs
- Meeting needs
- Utilizing creativity
- Lessons Learned

Moderator: Sam Ellis, Vice President, Biochemist, Thomson Instrument Co.

Panelists:

Joanne T. Beck, Ph.D., Senior Vice President, Pharmaceutical Development, Shire Pharmaceuticals

Wayne Froland, Ph.D., Associate Vice President, Center for Biopharmaceutical Manufacturing Sciences, Merck Manufacturing Division

Stefan Schmidt, Ph.D., M.B.A., Vice President, Process Science & Production, Rentschler Biotechnologie GmbH

Haripada Maity, Ph.D., Research Advisor, Eli Lilly and Company

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

7:00 End of Day

THURSDAY, AUGUST 6

8:00 am Registration and Morning Coffee

SCALING UP AND DOWN

8:25 Chairperson's Remarks

Stefan Schmidt, Ph.D., MBA, Vice President, GMP Operations, Rentschler Biotechnologie GmbH

8:30 Reducing the Biotech Process Information Gap in the 21st Century: 'Implementing Process Analytical Technologies at the Seed Expansion Stage for Bioprocess Development and Manufacturing of Biologics'

CASE STUDY *Jose R. Vallejos, Ph.D., Scientist I, Manufacturing Sciences and Technology (MS&T), AstraZeneca/ Medimmune*

Manufacturing of Biologics at the seed expansion stage can be further optimized. Utilizing optical patch-based sensors as Process Analytical Technologies (PAT), we were able to enhance the inoculum expansion stage by enabling T-flasks with Dissolved Oxygen and pH sensors. Our results show the potential of implementing PAT at the inoculum expansion stage to improve process understanding and to speed up process development, tech transfer, and process improvement timelines.

5th Annual

Bioproduction: Scale, Bioreactors & Disposables

Making It Work

9:00 Points to Consider When Scaling Up Raw Materials in Your Manufacturing Process

David Kolwyck, MBA, Director, Manufacturing Sciences, Raw Materials, Biogen Idec, Inc.

This presentation will review technical issues that can arise during the quantitative scale-up of raw materials due to changes in manufacturing scale or supplier sourcing of those raw materials. It is intended to provide guidance on technical issues to consider and discuss with suppliers during the scale-up of raw material demand to ensure consistent performance from pilot to large manufacturing.

9:30 Case Studies for Utilization of Conventional and CFD Approaches for Successful Scale Up and Scale Down of Bioreactor Processes for Monoclonal Antibodies

CASE STUDY *Michelle LaFond, Director, Bioreactor Scale-Up and Development, Regeneron Pharmaceuticals*

Use of both conventional and computational fluid dynamic approaches to develop scale-down, pilot-scale models of production bioreactors have resulted in improved process understanding and more successful transfer for late stage processes. The new scale-down models are more predictive of manufacturing and are used to map out impact of scale-up parameters and bioreactor type to process performance. Case studies of our approach to scale-up will be discussed.

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

BIOPRODUCTION STRATEGIES

10:45 Development of a Novel Feeding Strategy for an Industrial Yeast Strain

Simona Capone, Process Assistant, Chemical Engineering, Vienna University of Technology

I will present a bioprocess development strategy based on dynamics for an industrial yeast strain, which is induced under de-repressing conditions. A developed novel mixed-feed strategy gave 3 times higher space time yields than conventional feeding regimes.

11:15 HCCF Air Sparging for Prevention of Antibody Disulfide Bond Reduction

Melissa Mun, Senior Engineer, Genentech, Inc.

11:45 Effect of Microspargers on Product Quality Variability in Large-Scale Perfusion Bioreactors

Nirel Rillera, Research Associate II, BioMarin Pharmaceuticals, Inc.

Multivariate analysis on commercial processes suggested a relationship between superficial gas velocities and cell death, which coincided with variability in product quality attributes. In order to better control product quality, microsparger design was optimized for lower superficial gas velocities and reduced fouling susceptibility. After implementation at commercial scale, the new microspargers were successful in addressing fouling events and improved product quality control.

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

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

1:15 Close of Conference

Optimizing Cell Line Development

Enhancing Expression

THURSDAY, AUGUST 6

OPTIMIZING PROCESS DEVELOPMENT

1:55 pm Chairperson's Remarks

Christina Alves, Ph.D., Scientist, Cell Culture Development, Biogen Idec, Inc.

» 2:00 OPENING KEYNOTE PRESENTATION: The Future Looks Great… but What Is It?

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

Use of understanding developed through systems biology, coupled to the application of synthetic biology, will generate an exciting and brave manufacturing world in which novel CHO cell variants will be matched to expression of engineered unique biopharmaceutical entities … perhaps? I will give a personalized review of the reality of progress to date and how adoption of developing technologies has the potential to make a real difference.

2:45 Upstream Process Optimization, Automation and Collaboration: An Accelerated Path to the Clinic

Pamela Pegman, Ph.D., Senior Principal Scientist, Cell Line Development, Pfizer, Inc.

Optimizing cell line development activities has the potential to reduce the time and resources required for clinical entry. This presentation will summarize a combination of approaches to reduce cell line development timelines including creative timing of upstream activities through collaboration and harmonization with discovery partners, introduction of automation, and the use of business practice modeling to predict the best outcomes for key technology introduction.

3:15 Improving Stability through Vector Design

Thomas Jostock, Ph.D., New Technologies Network Leader / Novartis Leading Scientist, Novartis

3:45 Using Combinatorial Genome Editing to Improve Production in CHO Cells

Sponsored by horizon

Brian Burke, Ph.D., Business Development Director, Products, Horizon Discovery

Horizon have started a combinatorial gene editing program to improve CHO cell line performance. Together with the development of a high throughput reporter system we will generate a range of cell lines with different production traits to meet the future needs of biologics manufacture and develop next-generation production systems.

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

CELL LINE DEVELOPMENT FOR BACULOVIRUS

4:45 Engineering the Baculovirus Genome for Better Protein Production from Insect Cells

Dominic Esposito, Ph.D., Director, Protein Expression Laboratory, Frederick National Lab for Cancer Research

Protein production from insect cells using the baculovirus expression system has proven very useful for the generation of high-quality heterologous proteins when other systems have failed. However, insect cell protein production differs from mammalian expression due to differences in post-translational modification pathways. In order to overcome some of these differences, genome engineering of the baculovirus can be used to "humanize" insect cell protein production. We describe methods for facile modification of the baculovirus genome to both add new pathways for post-translation modification of proteins and also to enhance the stability of baculovirus constructs for protein production.

5:15 Optimizing Insect Cell Lines for Production of Structurally Uniform Glycoproteins

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

My presentation will cover previous, as well as more recent and ongoing efforts to produce insect cells with humanized glycoprotein processing pathways. Data will show recent efforts have yielded insect cell lines optimized for human-type protein glycosylation. Furthermore, data will show those cell lines can produce structurally homogenous glycoproteins.

5:45 End of Day

6:30-9:00 Recommended Dinner Short Course*

Transient Protein Production in Mammalian Cells

* Separate registration required; click here for details

FRIDAY, AUGUST 7

8:00 am Registration and Morning Coffee

CHO CLONE SELECTION & CELL LINE DEVELOPMENT

8:25 Chairperson's Remarks

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

» 8:30 FEATURED PRESENTATION: An Inducible System for the Rapid Generation of CHO Pools and Stable Clones

UNPUBLISHED DATA *Yves Durocher, Ph.D., Research Officer, Human Health Therapeutics Portfolio, Biologics & Biomanufacturing Program, National Research Council Canada*

Using the cumate-inducible promoter, we developed a CHO platform for the rapid generation of stable pools in less than 3 weeks post-transfection. The pools are stable over time and can be used to isolate stable CHO clones showing high productivities. We will provide examples of pools generated for the production of monoclonal antibodies, secreted and membrane proteins. This platform is a useful and cost-effective addition to the large-scale CHO transfection platform for the rapid production of recombinant proteins.

Optimizing Cell Line Development

Enhancing Expression

9:00 Screening of CHO Cell Clones by Mass Balance of Amino Acids

Wen Wang, Ph.D., Postdoctoral Associate, Chemical Engineering, Massachusetts Institute of Technology (MIT)

Post-transfection clone screening is a crucial step in mammalian cell line development for production of therapeutic proteins. Ideally, the screening should be non-invasive, economical, and effective. We report a fundamentally new method for predicting mAb titer in a Chinese hamster ovary (CHO) cell culture system based on mass balance of two essential amino acids. This study provides an alternative way to screen high therapeutic protein producers in a low-cost manner.

9:30 Stable Glycoengineering of CHO Cells

Claus Kristensen, Ph.D., Associate Professor, Copenhagen Center for Glycomics (CCG), University of Copenhagen

Recent advances in precise gene editing technologies such as ZFNs, TALENs and CRISPR/Cas9 systems have enabled stable engineering of mammalian cells to produce well-defined N and O-glycans. In this lecture we will present state-of-the-art glycoengineering in CHO to produce more homogeneous glycans and options for novel designed glycan structures.

10:00 Coffee Break

SYSTEMS BIOLOGY & HIGH-THROUGHPUT TECHNIQUES FOR DEVELOPING CELL LINES

10:45 Developing Systems Biology Models Based on Whole-Genome Sequencing of CHO to Guide Cell Line Engineering

Nathan Lewis, Ph.D., Assistant Professor, Systems Biology Research Group, University of California, San Diego

Our recent whole-genome sequencing efforts for CHO have enabled the construction of systems biology models of metabolism, protein secretion, and glycosylation. We now use these for detailed analysis of -omics data from CHO to deepen our understanding of differences between host cell lines and to guide our cell line engineering efforts. These efforts aim to enhance cell growth, tailor protein modifications, and improve protein secretion, in order to better control biotherapeutic critical quality attributes.

11:15 Utilizing High-Throughput Bioanalytics for Early Detection of Product Impurities

CASE STUDY *Christina Alves, Ph.D., Scientist, Cell Culture Development, Biogen Idec, Inc.*

Improvements in the throughput and efficiency of analytical techniques have enabled their use earlier on in the cell line development process. This in turn provides useful information on a large number of clones at a very early stage. In this case study we demonstrate how the use of these techniques allowed early detection of product impurities which in turn prevented delays in clinical timelines and the need for additional resources.

11:45 High-Throughput Product Quality Assays for Cell Line and Process Development

UNPUBLISHED DATA *Shashi Prajapati, Ph.D., Senior Scientist, High-Throughput Analytical Group, Cell Culture Development, Biogen Idec, Inc.*

Cell line and process development play a major role in producing therapeutic proteins with high productivity and appropriate product quality attributes. To support this development, analyses of large number of samples generated from thousands of clones and process optimization are critical. Analyzing large number of samples has been a bottleneck in biotech industries because conventional analytical assays are low-throughput. Here we present various high-throughput (HTP) analytical platforms to facilitate rapid and parallel analyses of product quantity and quality using 96-well plate formats. These platforms include HTP protein quantitation followed by HTP protein purification and product quality analyses. With these analytical capabilities, we can assess product quality in the early stage of clone screening, as well as expedite the cell line and process development.

12:15 pm Using Process and Activity to Drive Clone Selection

Sponsored by ARAGEN

Oren Beske, Ph.D., COO, Aragen Bioscience, Inc.

During a manufacturing cell line development project in stable CHO-K1 cells, a significantly reduced specific activity of target protein was observed when compared to a reference standard. This case study highlights how the lack of activity was identified and how the development of an optimized cell culture process enabled identification of high productivity clones.

12:30 Sponsored Presentation *(Opportunity Available)*

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

1:15 Session Break

INNOVATIVE TECHNOLOGIES & STRATEGIES

1:25 Chairperson's Remarks

Pamela Pegman, Ph.D., Senior Principal Scientist, Cell Line Development, Pfizer, Inc.

1:30 Development of Synthetic Biology Tools to More Predictably Clone, Express and Select Active Biologics in Cell Line Development

Ian Fotheringham, Ph.D., Managing Director, Ingenza Ltd.

In this talk, I will describe how Ingenza has developed and deployed various synthetic biology tools to enable us to more predictably clone, express and select active proteins during cell line development. I will use real-world examples of solving customer problems to illustrate the utility of our approach. These tools include protein engineering to address poor response kinetics during the control of gene expression, the development of synthetic "landing pads" to optimize the genomic operating environment, and the use of genome editing and RNA trafficking systems.

Optimizing Cell Line Development

Enhancing Expression

2:00 Enabling Evaluation of Polysaccharide Size and Content for DOE Studies in Early Process Phases

Erwin Swennen, Ph.D., Manager, Cell Line and Process Analytics, Bacterial Drug Substance Development, Novartis Vaccines

This talk presents the development of an innovative RP-SE(GPC) analytical method to monitor both critical quality attributes of GBS capsular PS during all phases of the production process. This method enabled DOE studies also in early process phases with complex matrix, and contains a practical approach on how industrial R&D is trying to keep up with the constant increase in quality requirements by regulatory agencies (QbD, DoE in early phases). The method represents a new out-of-the-box application of technology.

2:30 Development of Human Cell Systems for Evaluating the Responses of Drugs Directed at Correcting the Function of Cellular Proteins

Dieter Gruenert, Ph.D., Professor, Otolaryngology-Head and Neck Surgery, University of California, San Francisco

Our lab has been a leader in the development of these cell systems that have been used in academic and industry settings nationally and internationally. We have developed human airway epithelial and iPS cell systems to evaluate and screen the responses to drugs aimed at correcting the function of proteins involved in airway diseases such as cystic fibrosis.

3:00 Networking Refreshment Break

3:15 GlycoExpress: A Toolbox for the High Yield Production of Glycooptimized Fully Human Biopharmaceuticals in Perfusion Bioreactors at Different Scales

Rainer Stahn, Ph.D., Head, Bioprocess Development, Glycotope GmbH

GlycoExpress cells producing mAb are cultivated with perfusion bioreactor systems applying different cell retention mechanisms such as centrifugation (centritech) or alternating tangential flow (ATF) filtration at different scales. Growth, product yield and product quality, especially glycosylation, are evaluated during the cultivation. Perfusions culture helps to keep cells in the optimal growing and production phase over the production process which leads to highly stable product quality allowing a flexible duration of the run in one batch size.

3:45 Setting Pre-Work Priorities and KPIs to Avoid the Most Significant Challenges during Tech Transfer

Jayant Aphale, Ph.D., MBA, Senior Vice President, Technical Operations, Sarepta Therapeutics

Communication is essential before, during, and after the tech transfer process. Pre-tech transfer activities are critical in ensuring success of the tech transfer process. You must have the appropriate skill sets and competencies in place with all of your upstream / downstream partners so that you have understood any constraints and agreed on the scope of the work and acceptable parameters months before tech transfer begins.

4:15 Close of Conference

Overcoming Formulation Challenges for Biopharmaceuticals Development:

Formulation and Process Optimization, Analytics, Device Integration and New Biologics

MONDAY, AUGUST 3

8:00 am Pre-Conference Registration and Morning Coffee

9:00-11:30 Recommended Short Course* Accelerated Stability Testing of Biologics

* Separate registration required; click here for details

11:30 Main Conference Registration

UNDERSTANDING EXCIPIENTS STABILITY & PARTICLES IN BIOPHARMACEUTICALS

1:00 pm Chairperson's Opening Remarks

Sandeep Yadav, Ph.D., Scientist, Late Stage Pharmaceutical Development, Genentech, Inc.

» KEYNOTE PRESENTATION:

1:10 Polysorbate 80 Hydrolysis and Rationale for Determining the Effective Level of Polysorbate 80 in a High Concentration Monoclonal Antibody Formulation

UNPUBLISHED DATA *Vincent Corvari, Ph.D., Senior Research Advisor, Bioproduct Research & Development, Eli Lilly & Company*

During the development of a solution formulation for a high concentration monoclonal antibody, a reduction in the content of polysorbate 80 occurred on stability. Further evaluation demonstrated the reduction resulted from hydrolysis of the fatty acid side chains. The focus of this presentation is to describe the knowledge gained while identifying this degradation pathway and the development work conducted to define the effective level of polysorbate 80 required to maintain product quality.

» KEYNOTE PRESENTATION:

1:45 Is PS-80 a Critical Excipient? A Short History and Case Studies

CASE STUDY *Michael T. Jones, Ph.D, Research Fellow, Biotherapeutics Pharmaceutical Sciences, Analytical R&D, Pfizer, Inc.*

Polysorbates are ubiquitous as excipients in protein formulations. These surfactants are added to the formulation to help maintain the stability of the drug product (DP). There has been an increased interest in the biopharmaceutical industry to understand the fate of these surfactants over the shelf-life of the DP. This talk will highlight some of the issues with polysorbates and provide case studies on the criticality of PS80 addition to a protein DP.

2:15 Critical Considerations for Surfactant Stability in Biopharmaceutical Formulations

Sandeep Yadav, Ph.D., Scientist, Late Stage Pharmaceutical Development, Genentech, Inc.

Polysorbate is commonly used excipient in biotherapeutic formulations for protection against interfacial stress and surface adsorption. In this work we present evidence of Polysorbate degradation over long-term 5OC storage that may subsequently result into visible and subvisible particles in protein formulation. A number of challenges associated with characterizing particulates, identifying potential reasons for Polysorbate degradation, novel methods to quantify the degradants as well as the solubility characteristics of the PS20 degradants are discussed.

2:45 Refreshment Break

3:15 Challenges in Co-Formulating Polysorbates and Preservatives in Multi-Use Biologics Formulations

Shuai Shi, Ph.D., Associate Principal Scientist, Sterile Product and Analytical Development, Merck

The compatibility between polysorbates and m-cresol was thoroughly investigated in this study. It was found that both PS20 and PS80 are compatible with m-cresol (at 2.8 mg/mL) when their levels were not greater than 20 ppm. Significant losses of polysorbates were observed when PS20 and PS80 concentrations were above 50 ppm. Also, it was demonstrated that factors such as the presence of salt, the order of addition, and the hydrophobicity of surfactants could also impact compatibility. Furthermore, the agitation study demonstrated that even trace levels of PS20 and PS80 (e.g., 20 ppm) could stabilize the protein against fibrillation and aggregation.

3:45 Development of a Stability Indicating Assay for Polysorbate-80

UNPUBLISHED DATA *Mark Bolgar, Ph.D., Senior Research Fellow, Analytical and Bioanalytical Development, Bristol-Myers Squibb Co.*

The extreme heterogeneity of polysorbate 80 creates challenges for its quantitation in biotheraputic formulations. Ideally, any method should distinguish between intact PS-80 and key degraded forms. Of particular concern is the degradation of PS-80 via ester bond hydrolysis. This presentation will describe the development of LC/MS-based method for the determination of PS-80 which due to its very high specificity is able to effectively differentiate between intact PS-80 and its hydrolyzed forms.

4:15 Breakout Discussions

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

Topic 1: What Does It Take To Move A Formulation From Vials To Prefilled Syringes?

Moderator: Mark Yang, Ph.D., Director, Fill Finish Development, Genzyme - a Sanofi Company

- What are the most efficient ways to evaluate the device-ability of current formulations?

Overcoming Formulation Challenges for Biopharmaceuticals Development:

Formulation and Process Optimization, Analytics, Device Integration and New Biologics

- What are the "norms" for development timelines and budget?
- Key development steps/challenges to move from vials to prefilled syringes

Topic 2: What Constitutes A Critical Excipient?

Moderator: Michael T. Jones, Ph.D, Research Fellow, Biotherapeutics Pharmaceutical Sciences, Analytical R&D, Pfizer, Inc.

- Are specific excipients required for a stable formulation or would similar excipients work as well?
- What concentration of the excipient is required to guarantee it's function?
- At the end of shelf-life, does the DP still meet all of the specifications required regardless of excipients present?

Topic 3: Formulation Development of the Future – Can We Develop Better Formulations Faster?

Moderator: Russell Burge, Ph.D., Applications Scientist, Freeslate, Inc.

- Can automation help accelerate formulation development? What are the best approaches to continue with rapid and innovative formulation development?
- Are current analytics sufficient? What improvements are needed to provide better characterization faster?
- What are the best practices for implementing QbD in formulation development?

5:15 Discussion Report-Outs

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

7:00 End of Day

TUESDAY, AUGUST 4

7:30 am Registration and Morning Coffee

OVERCOMING FORMULATION CHALLENGES: QbD, PROCESS CHALLENGES & PRODUCT QUALITY

7:55 Chairperson's Remarks

Kevin Constable, Director, Technology Development, Terumo- Global Pharmaceutical Solutions.

8:00 Transformational Science: Moving from the Challenges of High Concentration mAbs to Meeting the Needs of Highly Potent Bispecifics

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

Glenmark's proprietary BEAT® technology has provided a new impetus toward developing a more efficient way of treating cancer. This highly effective therapeutic (anticipated doses ~ 1000 fold less than conventional mAbs) has conserved key IgG properties (thermostability, effector function/ antibody-like pharmacokinetics etc), but at the same time has thrown up new challenges, particularly in terms of formulation/analytical development. These low-concentration related challenges were rationally understood, characterized and mitigated.

8:30 Controlling Excipients during Commercial-Scale Formulation: Modelling-Based Control Strategy Design

CASE STUDY UNPUBLISHED DATA *Rachael Lewus, Ph.D., Scientist II, Formulation Sciences, MedImmune, Inc.*

Control of excipients during commercial scale formulation is important in order to deliver a high quality drug substance and ensure release criteria are met. However, an accurate scale down model for the excipient spiking step is not readily available for experimental characterization. Monte Carlo modelling provides an alternative method for process characterization. A case study focusing on polysorbate control in a monoclonal antibody drug substance formulation will be presented.

9:00 QbD in Late Stage Formulation Optimization

CASE STUDY UNPUBLISHED DATA *Mark Yang, Ph.D., Director, Fill Finish Development, Genzyme - a Sanofi Company*

QbD is a powerful tool for late stage formulation optimization and process definition. However, there is a delicate balance between testing many variables over a wide range for a robust process and minimizing the "process changes" to be implemented. A QbD case study will be presented. After identified key excipients, the formulation was optimized by using a response surface design to include multilevelsof key excipients over a manufacturing-relevant range.

9:30 Physical and Colloidal Stability Studies of mAbs and bi-Specifics

Sponsored by UNCHAINED LABS

Ralf Joseph Carrillo, Ph.D., R&D-GPMA Global Project Management, GPAS Global Pharmaceutical Analytical Sciences, Formulation, Abbvie

Biophysical properties of two monoclonal antibodies and two Dual Variable Domain Immunoglobulin (DVD-Ig™) proteins have been studied to ascertain how protein – protein interactions (B_{22}), unfolding and aggregation onset melting temperatures and turbidity demonstrate the propensity to predict both good and poor (aggregation and phase separation) mAb and DVD-Ig formulations.

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

Overcoming Formulation Challenges for Biopharmaceuticals Development:

Formulation and Process Optimization, Analytics, Device Integration and New Biologics

10:30 FEATURED PRESENTATION: Mixing Monoclonal Antibody Formulations Using Bottom-Mounted Mixers – Impact of Mechanism and Design on Drug Product Quality

CASE STUDY *Yuh-Fun Maa, Ph.D., Principal Engineer, Pharmaceutical Processing and Technology Development, Genentech, Inc.*

Although BMM is becoming a choice of mixing but impact of BBM on protein drug product is yet to be understood. This study evaluated multiple disposable BBMs to assess their impact on a shear-sensitive mAb formulation. Aggregation of mAb, and particle formation were determined after mixing. The results suggested that mixer designs with contact between the impeller and the drive unit resulted in higher particle counts. The shear-induced particles are proteinaceous but soluble aggregated protein molecules were not detected. This study fills an important gap in understanding a critical bioprocessunit operation.

11:00 Molar Mass, Size, Charge and Conformation: Light Scattering Tools for Biophysical Characterization of Macromolecules

Sponsored by WYATT TECHNOLOGY

John Champagne, Ph.D., Northeast Regional Manager & Senior Applications Scientist, Wyatt Technology Corporation

This seminar describes a comprehensive suite of characterization tools based on static and dynamic light scattering, which work together with size-based separation, to provide first principles biophysical characterization of macromolecules. Some of the key applications of the light scattering toolbox include analyses of molar mass and size distributions, aggregation, branching and other measures of conformation, and the composition of complex protein systems and other conjugated macromolecules.

11:30 Application of Automated and High-Throughput Systems to Formulation Development of Biopharmaceuticals

Sponsored by freeslate

Russell Burge, Ph.D., Applications Scientist, Freeslate, Inc.

Biologics can be prone to degradation and instability, both of which pose challenges to drug developers. In this presentation, we describe the application of automation and high throughput data management systems to drug development workflows. Results of case studies demonstrating the ability of automated workflows to increase throughput, improve efficiency, and streamline data management.

12:00 pm Panel Discussion: Challenges and Opportunities in QbD Approach in Formulation Development and Product Quality

Moderator: Mark Yang, Ph.D., Director, Fill Finish Development, Genzyme – a Sanofi Company

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

Rachael Lewus, Ph.D., Scientist II, Formulation Sciences, MedImmune, Inc.

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

Russell Burge, Ph.D., Applications Scientist, Freeslate, Inc.

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

1:15 Session Break

RAPID SCREENING OF FORMULATION STABILITY IN EARLY DEVELOPMENT

1:55 Chairperson's Remarks

Hardeep Samra, Ph.D., Senior Scientist, Formulation Sciences, MedImmune, Inc.

2:00 A Novel Analytical Approach to Investigate the Effect of Methionine Oxidation on Antibody PK

CASE STUDY *Jan Stracke, Ph.D., Principal Scientist, Pharmaceutical Development & Supplies, PTD Biologics Europe, F. Hoffmann-La Roche Ltd.*

Preserving the chemical and structural integrity of antibodies during manufacturing and storage is a major challenge during development. Oxidation of Fc methionines is frequently observed, which leads to reduced affinity to FcRn and faster plasma clearance if present at high levels. A novel pH-gradient FcRn affinity chromatography method was developed to isolate antibody oxidation variants from an oxidized IgG1 preparation based on their FcRn binding properties. The subsequent physico-chemical and biological characterization of these oxidation variants demonstrated the value of the new method to study structure-function relationships.

2:30 Developability Assessment and Formulations Optimization of Biologics Using Isothermal Chemical Denaturation (ICD)

Sponsored by UNCHAINED LABS

Richard K. Brown, Ph.D., Unchained Labs

Stability optimization and aggregation minimization are two of the most important hurdles in the development of biologics. ICD provides the most accurate way of measuring protein stability under different formulation conditions. ICD experiments performed at different protein conc. provide a quantitative assessment of protein aggregation in the native and denatured states. ICD is ideally suited to optimize the formulation of highly concentrated formulations, bispecific antibodies and antibody drug conjugates. In this talk, the fundamentals of ICD and its application to the evaluation of protein stability and optimization of formulation conditions will be discussed.

3:00 Sponsored Presentation *(Opportunity Available)*

Overcoming Formulation Challenges for Biopharmaceuticals Development:

Formulation and Process Optimization, Analytics, Device Integration and New Biologics

3:15 Poster Highlight Presentation: Leveraging Automation in Development of High Concentration Protein Formulations

Aastha Puri, M.Sc., Associate Scientist II, Drug Product Science & Technology, Bristol-Myers Squibb

Formulation development of high concentration products, brings a unique set of challenges, including the potential for increased physical and chemical stability risks, as well as challenges related to handling of viscous material. This work demonstrates the utility of new automation technologies in proficiently executing experimental workflows on a viscous high concentration protein formulation and assisting a data-driven decision making process as part of a material sparing, multi-well screening methodology.

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

4:15 A Comparison of Biophysical Characterization Techniques in Predicting Drug Product Stability

Andrew Semple, Scientist, Sterile Product and Analytical Development, Merck & Co.

To predict stability behavior, solution-mediated interactions (Colloidal, self-association propensity) and key molecular characteristics of ten formulated protein-therapeutics were compared to their stability at accelerated (25C and 40C) and long-term storage conditions (2-8C) as measured by size exclusion chromatography. Our results show that colloidal stability, self-association propensity, and conformational characteristics (exposed Trp) provide reasonable prediction of accelerated stability, with limited predictive value at 2-8C stability. Other measurements (e.g., thermal unfolding temperature) did not show any correlation.

4:45 HDX-MS Sheds Mechanistic Insights on Mutation Induced Changes in Physical Stability of an IgG1 mAb Engineered For Extended Serum Half-Life

CASE STUDY *Ranajoy Majumdar, Ph.D., Research Scientist, Biophysical Characterization, Biopharmaceutical Research and Development, Eli Lilly and Company*

A triple mutation in the CH2 domain of an IgG1 mAb intended to increase *in vivo* half-life resulted in decreased physical stability. Although the mutation induced minimal differences in H/D exchange kinetics at the mutation sites and the FcRn binding epitopes, it increased the flexibility of an established aggregation hotspot in the CH2 domain. This case study reinforces our understanding of the correlations between mAb physical stability and its local flexibility.

5:15 Close of Conference

6:00-8:30 Recommended Dinner Short Course*
Protein Aggregation: Mechanism, Characterization and Consequences

* Separate registration required; click **here** for details.

High-Concentration Protein Formulations:

Formulation, Manufacturing, Analytics, High Viscosity, Aggregation, Devices and Delivery

TUESDAY, AUGUST 4

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

Protein Aggregation: Mechanism, Characterization and Consequences

* Separate registration required; click here for details.

WEDNESDAY, AUGUST 5

7:00 am Registration and Morning Coffee

PROTEIN-PROTEIN INTERACTIONS & DEALING WITH VISCOSITY

8:05 Chairperson's Remarks

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

» KEYNOTE PRESENTATION:

8:15 Protein-Protein Solvation in High-Concentration Solutions

Thomas Laue, Ph.D., Professor, Biochemistry and Molecular Biology; Director, Biomolecular Interaction Technologies Center (BITC), University of New Hampshire

At high concentrations, proteins will distribute themselves in a manner that minimizes the system free energy. Mechanistically, this means that proteins will form an increasingly important component of the solvation shell around any given protein. The importance of considering protein-protein solvation for both single-protein solutions, as well as for mixtures of proteins, will be described, and experimental data showing these effects will be presented.

9:00 Viscosity in High-Concentration Protein Formulations

UNPUBLISHED DATA *Thomas Palm, Ph.D., Senior Research Investigator II, Drug Product Science and Technology, Bristol-Myers Squibb Co.*

At high protein concentration, small changes in concentration or pH that are within the typical specification range can have a significant impact on product viscosity. Likewise, product viscosity is significantly higher at storage temperature of 2-8 °C than it is at ambient temperature. Viscosity ranges of a model antibody and implications for formulation development, manufacturing, and device development will be discussed.

9:30 Cluster Formation in Dense Protein Solutions and Its Implications to Solution Viscosity

CASE STUDY *Yun Liu, Ph.D., Research Associate Professor/ Instrument Scientist, Chemical & Bimolecular Engineering/Center for Neutron Research, University of Delaware/National Institute of Standards and Technology*

Protein cluster formation in solutions is of fundamental interest for both academics and industries, and is very important for solution viscosity control in concentrated protein solutions. We will present our recent research efforts to directly identify the structures of small reversible protein clusters in monoclonal antibody solutions. The fundamental physical mechanisms of high viscosity in monoclonal protein solutions will be discussed within the context of our research examples.

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

FORMULATION & CMC CHALLENGES OF HIGH-CONCENTRATION PROTEIN FORMULATIONS

10:45 Preformulation Screening for Risk Mitigation during the Development of Biopharmaceuticals

CASE STUDY UNPUBLISHED DATA *Randall Mauldin, Ph.D., Scientist II, Protein Formulation and Process Development, Biogen Idec*

In order to address unmet patient needs, drug candidates are becoming more complex and delivered at higher concentration than ever before. Furthermore, aggressive CMC timelines necessitate the need for a rigorous assessment of early-stage drug candidates to de-risk future development. This talk will provide an overview of the challenges and strategies for characterizing the multidimensional formulation space of novel biopharmaceuticals with limited sample availability.

11:15 HESylation® - A Versatile Polymer Modification Technology Enabling High-Concentration Protein Formulations

Thomas Hey, Ph.D., Director, Biochemistry, Innovation Center Complex Formulations, Fresenius Kabi Deutschland GmbH

The attachment of the biodegradable and poorly immunogenic polymer hydroxyethyl starch (HES) to biologicals leads to increased efficacy by stabilization of the protein and prevention of renal excretion. The resulting conjugates show high solubility, but comparably low viscosity, allowing s.c. administration of highly concentrated solutions. In addition, HESylation® was used to develop next-generation ADCs allowing site-specific conjugation and higher payload density while maintaining excellent binding activity with the target protein and cancer cells.

Sponsored by TERUMO

11:45 Designing a Unique Drug Delivery Device for Viscous Drug Products with Novel Needle Technology and Polymer Syringes

Kevin Constable, Director, Technology Development, Terumo- Global Pharmaceutical Solutions

New drug products being developed today are often created as concentrated proteins which can result in a viscous solution that may require novel devices for drug delivery. Using a systems approach to device design, we will explore how the combination of a silicone oil free polymer syringe system with a tapered needle can be combined to reduce the force of injection, improve functionality, and reduce the potential degradation of these complex protein based formulation.

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

High-Concentration Protein Formulations:

Formulation, Manufacturing, Analytics, High Viscosity, Aggregation, Devices and Delivery

1:30 Session Break

FORMULATION & CMC CHALLENGES OF HIGH-CONCENTRATION PROTEIN FORMULATIONS (cont.)

1:55 Chairperson's Remarks

Thomas Palm, Ph.D., Senior Research Investigator II, Drug Product Science and Technology, Bristol-Myers Squibb Co.

2:00 Drug Product Design and High Concentration Formulation Development

CASE STUDY *Bruce Kerwin, Ph.D., Head, Drug Product Design, Just Biotherapeutics, Inc.*

Protein formulation development is an evolving field that now encompasses the concept of drug product design rather than focusing solely on stabilization and concentration of the protein. Increasingly, an integrated approach to drug product design encompasses *in silico* tools, high throughput screening and development of predictive tools that integrate with the commercialization process. At this meeting examples and ideas will be combined to provide a vision of the future as it evolves into the field of drug product design.

2:30 CMC Strategies on Scaling Up and Down for High-Concentration Protein Formulations

Jamie Tsung, Ph.D., Principal Scientist, Momenta Pharmaceuticals, Inc.

Highly concentrated therapeutic proteins are prone to be viscous and aggregate posing developmental and CMC challenges in purification, formulation, analytical development, manufacturing, product stability, syringeability and injectability. This talk provides a review of current strategies and technologies used in product development to overcome these CMC challenges and minimize the impact on product quality.

3:00 Aromatic Amino Acid Salts Rescue the Solubility of a Poorly Soluble Multivalent Protein

CASE STUDY UNPUBLISHED DATA *Yu (Eunice) Tang, Ph.D., Principal Scientist, Drug & Combination Product Development Group, Shire HGT*

A multivalent protein demonstrates poorly solubility across wide pH range with temperature dependency. Conventional "salt in" ions further facilitate the precipitation of the protein. Interestingly, aromatic amino acid salts successfully rescue the protein solubility. A systemic investigation was performed to reveal the cause of the poor solubility and the mechanism of solubility enhancement by aromatic amino acid salts.

3:30 Simplest Concepts and Measurements May Become Challenges at High Protein Concentration

Erinc Sahin, Ph.D., Sr. Research Investigator, Drug Product Science & Technology, Bristol-Myers Squibb Co.

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

PLENARY SESSION

4:45 Chairperson's Remarks

Sam Ellis, Vice President, Biochemist, Thomson Instrument Co.

» 4:50 PLENARY KEYNOTE PRESENTATION:
Meeting the Needs of Patients with Rare Diseases: Innovation in Product Development

Joanne T. Beck, Ph.D., Senior Vice President, Pharmaceutical Development, Shire Pharmaceuticals

At Shire, where the delivery of innovative medicines to patients with rare diseases and other specialty conditions is a fundamental component of the business model, creative solutions are critical to our success. Starting with the transition of drug candidates from discovery research to the clinic, followed by late phase development and eventually commercial product lifecycle management, scientists and engineers focus on both technology innovation and creative business approaches to deliver high quality therapies to the patients while decreasing development timelines and costs.

5:20 Interactive Panel Discussion: How to Innovate Product Development

- Technologies
- Strategies
- Cutting Costs
- Meeting needs
- Utilizing creativity
- Lessons Learned

Moderator: Sam Ellis, Vice President, Biochemist, Thomson Instrument Co.

Panelists:

Joanne T. Beck, Ph.D., Senior Vice President, Pharmaceutical Development, Shire Pharmaceuticals

Wayne Froland, Ph.D., Associate Vice President, Center for Biopharmaceutical Manufacturing Sciences, Merck Manufacturing Division

Stefan Schmidt, Ph.D., M.B.A., Vice President, Process Science & Production, Rentschler Biotechnologie GmbH

Haripada Maity, Ph.D., Research Advisor, Eli Lilly and Company

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

7:00 End of Day

THURSDAY, AUGUST 6

8:00 am Registration and Morning Coffee

ANALYTICAL STRATEGY FOR HIGH-CONCENTRATION PROTEIN FORMULATIONS

8:25 Chairperson's Remarks

Bruce Kerwin, Ph.D., Head, Drug Product Design, Just Biotherapeutics, Inc

8:30 Building a Better Bridge: Biophysical Tools to Better Understand the Complexities of High Concentration Biotherapeutics

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

The thermodynamic interactions that govern a

High-Concentration Protein Formulations:

Formulation, Manufacturing, Analytics, High Viscosity, Aggregation, Devices and Delivery

variety of protein therapeutic and solution properties are distinctly protein concentration dependent. Manufacturing and dosing of therapeutic monoclonal antibodies frequently calls for high protein concentration solutions and the resulting non-ideality complicates reliable estimation of critical properties from measurements under dilute conditions. We illustrate the utility of different biophysical tools in bridging the dilute - high concentration gap by characterizing two antibodies that exhibit contrasting concentration-dependent behavior.

9:00 Challenges with Measuring Detergents and Excipients Used in Biopharmaceuticals

Shiranthi Jayawickreme, Ph.D., Associate Director, Analytical Development, Biogen Idec

A variety of detergents are used for solubilization, viral-inactivation, and as excipients in Biopharmaceutical drug substances and products. Lack of chromaphores in many of these detergents poses a challenge for the detection and quantitation of these components during process development and quality control. Current methods available for the determination of low levels of polysorbates in high concentration drug substances and drug products will be presented. Sensitivity and robustness of three different methods will be discussed.

9:30 Characterization of and Relationship between Soluble and Insoluble Aggregate Populations

Ronald Maurer, Ph.D., Scientist, Process Development – Downstream, Bristol-Myers Squibb Co.

Protein aggregation presents serious challenges in all stages of biotherapeutic development, compromising both product yield and patient safety. However, many fundamental aspects of aggregation are poorly described and prevent robust characterization and prediction of aggregation behavior. In this work, we investigate the relationship, if any, between soluble and insoluble protein particle formation and correlate their growth and stability to experimentally-tenable biophysical properties.

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

DELIVERY & DEVICE APPROACHES IN HIGH-CONCENTRATION / HIGH-VOLUME PROTEIN FORMULATIONS

10:45 Device & Formulation – Two Inseparable Aspects of a Successful Product

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

The biologics market is becoming increasingly competitive with multiple products competing for the same indication and a number of biosimilars in development. Therefore, there is a strong pressure for product differentiation offering distinct advantages over other products. Stability together with a convenient injection device are two key aspects of successful products. This talk will focus on unique formulation strategies and related device choices that enable development of competitive biopharmaceuticals.

11:15 Reconstitution of Highly Concentrated, Dried Proteins: What Have We Learned in the Past 5 Years?

Bakul Bhatnagar, Ph.D., Principal Scientist, Formulation & Process Development, Pfizer, Inc.

The reconstitution time of lyophilized biopharmaceuticals is a quality attribute where it is desirable and often critical to achieve fast reconstitution (for example, in an emergency environment) without compromising the product quality. The reconstitution times of highly concentrated freeze-dried proteins can be often quite long. The presentation will address recent advances in our understanding of the dissolution behavior and will cover aspects of mechanisms contributing to reconstitution, strategies to obtain rapid reconstitution, and methods to determine the end of reconstitution.

11:45 Adocia Viscosity Reducers (AVRs®) – A New Alternative to Reduce the Viscosity of Highly Concentrated mAb Formulations

Emmanuel Dauty, Ph.D., Head of the Physico-Chemistry Department, Adocia

Highly concentrated monoclonal antibody (mAb) formulations are often highly viscous, which poses manufacturing and administration challenges. Adocia has developed two distinct families of small molecules that have impressive viscosity-reduction properties in highly concentrated mAb formulations – Adocia Viscosity Reducers (AVR®). Through low-affinity electrostatic and hydrophobic interactions, AVR® excipients are capable of disrupting the mAb-mAb interaction network responsible for the high viscosity of highly-concentrated mabs, resulting in significant viscosity reduction.

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 June 26, 2015.

- 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
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High-Concentration Protein Formulations:

Formulation, Manufacturing, Analytics, High Viscosity, Aggregation, Devices and Delivery

12:15 pm Crystalomics – A Strategy for High-Concentration Protein Formulation

Sponsored by ALTHEA

Tan Leminh, MBA, Director, Technology Transfer, Althea

Crystalomics® is a technology platform that offers a formulation solution for protein therapies that must be delivered at high concentrations or as sustained release formulations. The technology can be used to formulate antibodies to up to 350 mg/ml, allowing IV infusions to be converted to SC injections. Crystalomics® is an ideal technology to formulate "BioSuperior" biologics that deliver superior dosing regiments and expanded patent protection for established protein therapeutics.

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

1:15 Close of Conference

Advances in Purification Technologies:

Novel Advances and Continuing Improvements for Higher Downstream Productivity and Purity

THURSDAY, AUGUST 6

NOVEL AND ALTERNATIVE APPROACHES TO PURIFICATION AND AGGREGATE REMOVAL

1:55 pm Chairperson's Remarks
Yi Li, Ph.D., Sr Scientist, Biologics Process Development, Bristol-Myers Squibb

» 2:00 KEYNOTE PRESENTATION
How to Scale-Up Precipitation of Recombinant Antibodies
Alois Jungbauer, Professor, Department of Biotechnology, BOKU and Head of Bioprocess Engineering, Austrian Centre of Industrial Biotechnology

Precipitation and flocculation has been considered as potential methods for capture of antibodies especially when perfusion culture is used for production. Ethanol precipitation and precipitation by non-charged polymers reached equilibrium in less than 1 minute. As rectors for such fast operations tubular reactors have been studied. As scale-up criteria fractal dimension of the flocks have been used. Mechanical compression during harvesting is influenced by dissolution kinetics.

2:45 Fatty Acid Extraction Of Chromatin Heteroaggregates From Mammalian Cell Culture Harvests
UNPUBLISHED DATA *Wei Zhang, Ph.D., Research Scientist, Downstream Processing, Bioprocessing Technology Institute, Singapore*

Saturated and unsaturated fatty acids ranging in chain length from 6 to 12 carbon atoms were evaluated over a range of pH and conductivity values to identify the combinations supporting the most effective reduction of aggregates, product-related impurities, and host contaminants while conserving high recovery of native IgG. Sensitive analytical methods were also developed. Results will be presented tracking contaminants and fatty acids through several 2-step IgG purification processes.

3:15 Development of Robust Impurity Clearance Methods Using Chromatographic and Non-Chromatographic Techniques
CASE STUDY UNPUBLISHED DATA *Srinivas Chollangi, Ph.D., Scientist II, Biologics Process Development, Bristol-Myers Squibb*

Sponsored by REPLIGEN

3:45 Production Scale Pre-Packed Chromatography for Use with 1000L & 2000L Bioreactors
Fletcher Malcom, MBA, Associate Director, Product Management, Repligen

How do we scale pre-packed chromatography to production-scale? The OPUS® 45 and 60 cm columns can purify a feed stream from 1000L - 2000L bioreactors. We will show how the unique design of these GMP-scale columns deliver equivalent or better performance as self-packed glass columns, and demonstrate how usage can result in substantial time and cost savings.

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

4:45 High Pressure Refolding as an Alternative Technology for the Manufacture of Biopharmaceuticals
CASE STUDY *Linda Gombos, Ph.D., Postdoc, Institute of Biotechnology (BOKU), Process Science Downstream Processing, BOKU-Boehringer Ingelheim RCV*

We evaluated the application of high hydrostatic pressure for refolding a variety of biopharmaceuticals. Our aim was to systematically compare this emerging technology to conventional refolding and to identify its potential economic benefits. We also compared the structure and activity of the two protein variants to address concerns on therapeutic effect and safety. Our results indicate that high-pressure is a potent technology for refolding proteins with significantly higher productivity and in unaltered quality compared with conventional refolding techniques.

5:15 Investigation of Fouling Mechanism of Hydrophobic Interaction Chromatography Resin during Monoclonal Antibody Purification
UNPUBLISHED DATA *Theodore T. Diakov, MSc, Associate Scientist, Downstream Process Development, Bristol-Myers Squibb*

Fouling of chromatography resins during repeated cycles of use can be a significant problem as it can compromise the capacity to clear impurities as well as cause inconsistent performance. Identifying the fouling species and mechanism can provide valuable understanding and assist in designing more efficient cleaning strategies. In this work we examined fouling of hydrophobic interaction chromatography resin during a monoclonal antibody purification process. Historically, HIC resins have been shown to allow protein unfolding on the surface under favorable conditions and we propose that protein deposits adsorbed by this mechanism are exhibiting resistance to traditional cleaning approaches. We report our comparisons of the resin performance in fouled and non-fouled state, the results of our pursue in identifying the nature of the foulant and its localization within the resin and our approaches in cleaning.

5:45 End of Day

6:30 - 9:00 Recommended Dinner Short Course*
SC10: Anything but Chromatography – Precipitation, Crystallization and Flocculation
* Separate registration required; click here for details.

Advances in Purification Technologies:

Novel Advances and Continuing Improvements for Higher Downstream Productivity and Purity

FRIDAY, AUGUST 7

8:00 am Registration and Morning Coffee

PURIFICATION OF NEW & COMPLEX FORMATS

8:25 Chairperson's Remarks

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

8:30 Modular Approaches to Express and Purify Complex Therapeutic Proteins

Stefan Schmidt, Ph.D., Vice President DSP Production, Rentschler Biotechnologie GmbH

Difficult to express proteins represent an increasing amount of therapeutic molecules. This causes bioprocessing challenges such as controlling glycosylation, increasing titers and yields and suppressing aggregation. Here I demonstrate how to develop modular processes based on DoE principles solving these issues. Various case studies highlight successful process design, optimization strategies and critical manufacturing parameters. Additionally practical advice will be given on what to consider when designing a novel molecule.

9:00 Single Step Purification of Biotherapeutic Proteins in a Highly Simplified Process Using an Optimized, Proprietary Fragment Complementation System

David O'Connell, Ph.D., Lecturer, Director, MSc Programmes, Biotechnology, School of Biomolecular & Biomedical Research, University College Dublin

Engineering of a very high affinity complementation between two calcium-binding protein domains has led to the development of a robust purification system that in a single step produces high yields of very pure protein for downstream analysis, dispensing with time consuming dialysis step. Through collaborations with leading biopharmaceutical companies and research institutes the purification of proteases, kinases and binder proteins will be presented.

9:30 Assembly of Knob and Hole Bispecific Antibodies

Josefine Persson, Ph.D., Senior Group Leader, Purification, Genentech, Inc.

We have produced glycosylated and aglycosylated CHO and *E. coli* Knob & Hole Bispecific Antibodies. In all cases the assembly conditions and assembly effectiveness are very similar. Our data shows that the assembly step is very robust and efficient in producing the Knob & Hole Bispecific Antibodies while minimizing the amounts of homodimers (mAb).

10:00 Coffee Break

10:45 The Challenges of Developing Processes for New Protein Formats

Andreas Schaubmar, Ph.D., Head of Downstream Processing, Large Molecule Research, Roche Pharmaceutical Research and Early Development, pRED, Roche Innovation Center Penzberg

Innovative biologics often combine several protein domains in increasingly complex formats to achieve superior therapeutic effects. We developed manufacturing processes for several new formats that provide the required yield and purity for clinical studies. For that we considered the design of the therapeutic format and integrated the selection of a suitable cell line, the development of a productive fermentation process and a complementary purification scheme in a process effectively minimizing product related impurities.

11:15 Scaling-Up of a Downstream Purification Process for a New Recombinant Product (rhFVIII)

Martin Linhult, Ph.D., Head of Bio100 line 1, Octapharma

Octapharma has developed a new process for the production of a recombinant human FVIII product derived from a human cell line (HEK293F cells). Clinical trials are ongoing with positive results. During process development several different approaches have been tested, old established techniques as well as new ones has been evaluated. In this presentation I will discuss scale-up of a new downstream purification process and also different affinity ligands that could be applied.

11:45 Purification of a Highly Disulfide Linked Protein by Cation Exchange Chromatography

Thomas Linke, Ph.D., Senior Scientist, Purification Process Sciences, MedImmune

We present an informative case study on the development of a direct capture step of a refolded, novel biotherapeutic by ion exchange chromatography without prior buffer exchange. High yield and product purity in a single step made it possible to replace two affinity columns used in the pre-clinical manufacturing process. Low solubility in solution and a propensity toward aggregation presented special challenges for process development.

12:15 pm Sponsored Presentation
(Opportunity Available)

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

1:15 Session Break

PURIFICATION OF MEMBRANE PROTEINS AND ANTIGENS

1:25 Chairperson's Remarks

Julie Bomholt, Ph.D., Protein Specialist, Research & Development, Aquaporin A/S

1:30 Membrane Proteins: From Lab-Scale towards Large-Scale Production

CASE STUDY UNPUBLISHED DATA *Julie Bomholt, Ph.D., Protein Specialist, Research & Development, Aquaporin A/S*

Downstream processing of membrane proteins is further complicated by the amphipathic nature of membrane proteins that even in the purified form are ternary complexes consisting of protein, lipid and detergent in unknown ratios. By use of the physiologically important trans-membrane protein family of aquaporins as model proteins, we developed a *S. cerevisiae*-based expression system and identified conditions that allowed us to substantially increase the membrane density of recombinant functional aquaporin.

2nd Annual

Advances in Purification Technologies:

Novel Advances and Continuing Improvements for Higher Downstream Productivity and Purity

2:00 Antigen Purification for Biologics Projects

CASE STUDY *Medha J. Tomlinson, Ph.D., Senior Scientist, Global Biologics – Protein Sciences, Abbvie Bioresearch Center*

The early discovery stage of antibody programs requires generation of proteins and cell lines. Appropriate construct design and expression systems are needed to retain antigen biophysical characteristics and activity. Proprietary antibody generation requires expression and purification of various orthologues for screening and optimizing affinity. Rapid turnaround and antigen supply are paramount for success. This talk will focus on working towards building a robust platform to overcome many of these challenges.

MINIATURIZATION AND AUTOMATION

2:30 Miniaturized and Automated Inclusion Body Processing – From Homogenization to Purification

CASE STUDY UNPUBLISHED DATA *Cornelia Walther, Ph.D., Post-Doc, Institute of Applied Microbiology/ Biopharma Austria Process Science, University of Natural Resources and Life Sciences Vienna*

Biopharmaceuticals overexpressed in *E. coli* are often deposited as high density aggregates in inclusion bodies requiring additional process steps such as inclusion body recovery, solubilization and refolding. For each product, individual needs of the process might present a bottleneck during downstream processing. We present a miniaturized platform for parallel screening of cell disruption, IB washing, solubilization and refolding conditions and purification compatible with the concept of DOE.

3:00 Networking Refreshment Break

SCALED-DOWN PROCESSES AS PREDICTIVE MODELS FOR LARGE SCALE PRODUCTION

3:15 Scaled-Down Model Qualification and Use for Process Improvement

Adam J. Meizinger, Ph.D., BS, Process Engineer II, Manufacturing Science and Technology Laboratory, Genzyme, A Sanofi Company

3:45 Challenges in Developing Predictive Downstream Scaled-Down Models

Omkar Joshi, Ph.D., Head, Downstream Development, Global Biologics, Bayer Healthcare

4:15 Close of Conference

This Conference is also part of: STREAM #4: Process Innovations & Cell Therapeutics

Click **here** for details.

Rapid Methods to Assess Quality & Stability of Biologics:

Improving Prediction and Screening

MONDAY, AUGUST 3

8:00 am Pre-Conference Registration and Morning Coffee

9:00-11:30 Recommended Short Course*
Biophysical Characterization in Assessing the Higher Order Structure (HOS) Fingerprint of Biopharmaceuticals
* Separate registration required; click here for details

11:30 Main Conference Registration

CHALLENGES AND OPPORTUNITIES FOR NEW METHODS FOR TESTING QUALITY &STABILITY

1:00 pm Chairperson's Opening Remarks
Jianmei Kochling, Ph.D., Director, Quality Science and Analytical Technology, Genzyme - a Sanofi Company

» 1:10 KEYNOTE PRESENTATION: Introducing Emerging Technologies into the QC Laboratory
CASE STUDY *Paul Bigwarfe, Ph.D., Director, Analytical Sciences, Regeneron Pharmaceuticals, Inc.*
Introducing new and emerging technologies to the QC laboratory presents its own set of challenges. Regulatory hurdles and training are only a few of them. This presentation will address how to overcome these challenges and present case studies on where it has worked and not worked well.

1:45 Emerging Technology for Biologics Stability Testing
Jianmei Kochling, Ph.D., Director, Quality Science and Analytical Technology, Genzyme - a Sanofi Company
Biologics are monitored for purity, potency, and biological activity in stability. The use of appropriate stability-indicating physicochemical, biochemical, and immunochemical analytical methodologies permits a comprehensive characterization and monitoring the quality of the drug substance and/or drug product. The effort of introducing advanced technologies to the QC labs has positively impacted the industry, leading to improved throughput, accuracy, precision, and sensitivity, as well as reduced labor and cost. Talk will discuss some recent changes in the QC world.

2:15 A Unique High Throughput Assay for Determination of the Potency and Stability of Biologics
CASE STUDY UNPUBLISHED DATA *Michael Tovey, Ph.D., INSERM Director of Research, Laboratory of Biotechnology and Applied Pharmacology, Ecole Normale Supérieure de Cachan, France*
Biologic activity is essential for the assessment of potency and stability of biologics and successful development of biologics depends upon establishment of validated and standardized assays that allow direct comparisons of the relative potency and stability between batches. A validated standardized high throughput assay platform using engineered reporter-genes allows direct comparison of drug potency and stability within two hours for structurally diverse TNF-α antagonists or closely related novel forms of human insulin and FGF-21.

2:45 Refreshment Break

3:15 Challenges to Implementing High Throughput Methods in a QC Environment
UNPUBLISHED DATA *Michelle Joubert, Staff Scientist, Genzyme a Sanofi Company*
Capillary electrophoresis using Beckman Coulter's PA 800 and the Caliper Labchip® GXII instruments are two platforms used to evaluate the purity of biologics. These platforms have a higher throughput than SDS-PAGE, as well as the ability to return quantitative results. Analytical methods using these technologies have been established for the analysis of products in early stages of development. Challenges and opportunities of implementing these methods in a QC environment will be discussed.

3:45 Analytical Testing Strategy for Admixture Testing of Therapeutics
Shenjiang Yu, Ph.D., Associate Principal Scientist, Sterile Product and Method Development, MRL, Merck Co. & Inc.
A pharmaceutical admixture consists of a drug product mixed with a suitable diluent in a intended dosing/delivery device for the purpose of parenteral infusion to the patient. Regulatory agencies have specific requirements for the demonstration of the compatibility of the drug product with reconstitution diluents, because many of the therapeutic proteins are dosed intravenously in the form of admixtures. Therefore, analytical strategies are presented to show the compatibility with dosing/delivery device. A few case studies is discussed with the implementation of our analytical strategies.

4:15 Breakout Discussions
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. Then continue the discussion as you head into the lively exhibit hall for information about the latest technologies.

Topic 1: What are Current Control Strategies for Submicron and Subvisible Particles in Biologics?
Moderator: Nataliya Afonina, Ph.D, President and Principle Consultant, AN Biologics Consulting LLC
- How protein aggregation in 0.1 -10 µm particle range may impact CQA related to product quality and purity?
- What are regulatory expectations?
- How industry is handling and controlling subvisible and submicron particles?

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Topic 2: Commercial Release Specification Setting

Moderator: Paul Bigwarfe, Ph.D., Director, Analytical Sciences, Regeneron Pharmaceuticals, Inc.

- Control strategies for various product forms/production stages
- What tests are necessary?
- Justification of acceptance criteria

Topic 3: High-Throughput and High Resolution Screening to Assess Physical and Chemical Instabilities in Protein

Moderator: Ranajoy Majumdar, Ph.D., Research Scientist, Biophysical Characterization, Biopharmaceutical Research and Development, Eli Lilly and Company

- What is the predictability correlation from in early development to late stage?
- Are there stability indicating techniques that correlate with shelf-life and in-use stability?
- Does the success of early phase stability prediction depend on product modality?
- How should an early stage stability screen look like to provide maximum knowledge for development?

Topic 4: Admixture Testing Strategy

Moderator: Shenjiang Yu, Ph.D., Associate Principal Scientist, Sterile Product and Method Development, MRL, Merck Co. & Inc.

- Clinical support and regulatory expectation
- Analytical tool box and strategy
- Special analytical development and investigation

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

7:00 End of Day

TUESDAY, AUGUST 4

7:30 am Registration and Morning Coffee

PROTEIN AGGREGATION, PARTICLES & STABILITY

7:55 Chairperson's Remarks

Joël Richard, Ph.D., Senior Vice President Peptides, Technical Operations, Ipsen

8:00 Strategy for Characterization and Control of Submicron and Subvisible Particles in Biologics

Nataliya Afonina, Ph.D., President and Principle Consultant, AN Biologics Consulting LLC

Aggregation of proteins, including formation of submicron (0.2 -2 µm) and subvisible (2 -10 µm) particles, is one of the major concerns in biologics drug products related to their stability, purity, and quality and is defined as Critical Quality Attribute. Finding the right risk-based approach and establishing the tractability between particle evaluation at formulation step and in final drug product is critical. New strategic approach for 0.2 -10 µm particle characterization and control including regulatory requirements, evaluation of orthogonal methods, and establishing of morphological libraries for subvisible particles will be discussed.

8:30 Addressing the Gaps in Particle Measurements for Biotherapeutic Solutions

UNPUBLISHED DATA *Reema Raghavendra, MS, MBA, Scientist II, Global Protein Sciences, AbbVie, Inc.*

Non-native protein structures, which are increasing in use, have potentially altered propensities to self-associate. Concerns regarding the immunogenicity of protein aggregates motivate particle characterization in the sub-visible range (0.1-100 µm). Flow cytometry holds the promise of distinguishing between particle types for sizes down to less than 1 µm. Here, we present two methods of standardizing flow-cytometry diameter readings: the use of novel protein-like standards of discrete sizes and commercial beads.

9:00 Stability Challenges for Protein Therapeutics: Anticipating Aggregation Phenomena at Early Development Stage

CASE STUDY *Joël Richard, Ph.D., Senior Vice President Peptides, Technical Operations, Ipsen*

The paradigm of protein formulation development has moved from a posteriori detection and control of aggregation to the anticipation/prediction of formulation, storage and processing conditions that will lead to aggregation in a QbD approach. In order to anticipate potential aggregation issues, it is proposed to focus on the early steps of aggregation, which most of the time may involve higher order structure (HOS) alterations and loss of colloidal stability.

Sponsored by sensiQ

9:30 For the First Time, Simultaneous Detection of Protein Aggregation and Affinity Measurements in the Same Single SPR Experiment

Aaron Martin, Senior Principal Scientist, SensíQ Technologies Inc

No technologies have been capable of delivering information on both drug affinity and protein aggregation simultaneously in the same experiment. SensiQ presents data from a collaboration with Genentech where this limitation is overcome by simultaneously detecting protein aggregation and determining affinity in the same experiment using Pioneer FE SPR instrumentation.

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

10:30 Investigate Protein Aggregation in Process Change through Forced Degradation Studies

UNPUBLISHED DATA *Yimin Hua, Scientist II, Quality Science and Analytical Technology, Genzyme, a Sanofi Company*

Aggregation is one of the main concerns of biotherapeutics when there is a process change. Detection and characterization of aggregation to identify the root cause will allow appropriate actions

Rapid Methods to Assess Quality & Stability of Biologics:

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which will help to improve protein quality, minimize protein aggregation during process and on storage. Proteins are subjected to different stress conditions to induce aggregation in the lab. Various analytical techniques will be used to characterize the forced degraded protein samples. The results will further the understanding of leading factors that contribute to the aggregation of recombinant proteins.

POST-TRANSLATIONAL MODIFICATIONS

11:00 Fast LC/MS Methods for Monitoring Sites of Modification in Development, PC/PV and Beyond

Amy Hilderbrand, Ph.D., Technical Development Scientist, Protein Analytical Chemistry, Genentech, Inc.

Being able to monitor site specific modifications in biological molecules is important from a process, stability and quality perspective in development. This talk will focus on rapid relative quantitation using liquid chromatography/mass spectrometry methods that are being evaluated and used to monitor sites that are vulnerable to modification.

11:30 High-Throughput Peptide Mapping to Support Early Prediction of Biologics Quality

UNPUBLISHED DATA *Yan Wang, Ph.D., Scientist, Analytical Development, Biogen Idec*

Peptide mapping is a sensitive and precise technique that is capable of detecting single amino acid changes and post-translational modifications (PTMs) in a single run. We have recently developed a novel high-throughput (HT) peptide mapping workflow, which targets four bottle-neck problems and enables analyst to complete multiple sample comparison in a single day starting from cell harvest to final quantitative report. Our new HT peptide mapping workflow is transferrable to assess quality of biologics in manufacturing, cell lines development and formulation development.

12:00 pm Poster Highlight Presentation: Determination of Multiple Product Attributes With a High-Throughput Automated Purification Assay

Jasmine Wang, M.S. Associate Scientist II, Analytical Biotechnology, MedImmune, Inc.

A high-throughput assay was developed and automated for the determination of multiple product attributes of monoclonal antibodies in conditioned medium. The samples containing monoclonal antibodies in conditioned media were purified using Protein A affinity magnetic beads and analyzed for multiple quality attributes, including fragmentation, aggregation, oligosaccharides, charge isoform levels, oxidation, deamidation, and other chemical degradation. Results on protein recovery and product quality attributes under various optimizing conditions will be presented. This high-through-put integrated platform allows rapid and efficient sample processing of up to 96 samples in three hours, and allows monitoring multiple quality attributes of IgG1, IgG2, and IgG4 during upstream process development.

12:30 Luncheon Presentation: iCE3: A Powerful Analytical Tool for Protein Charge Heterogeneity Characterization

Sponsored by proteinsimple

Jiaqi Wu, Principal Scientist, Biologics, ProteinSimple

Traditional tools for quantitative protein charge characterization include IEC and conventional cIEF. However, these tools have limited application for analyzing complex therapeutic proteins. Whole column detection cIEF instrument, iCE3, does not require mobilization of the focused bands. Its open capillary minimizes unspecific protein interactions with column. iCE3's fast speed increases throughput and minimizes sample precipitation and aggregation during IEF. iCE3 is the best tool for quantitative analysis of charge heterogeneity of complex proteins.

1:15 Session Break

RAPID SCREENING OF FORMULATION STABILITY IN EARLY DEVELOPMENT

1:55 Chairperson's Remarks

Hardeep Samra, Ph.D., Senior Scientist, Formulation Sciences, MedImmune, Inc.

2:00 A Novel Analytical Approach to Investigate the Effect of Methionine Oxidation on Antibody PK

CASE STUDY *Jan Stracke, Ph.D., Principal Scientist, Pharmaceutical Development & Supplies, PTD Biologics Europe, F. Hoffmann-La Roche Ltd.*

Preserving the chemical and structural integrity of antibodies during manufacturing and storage is a major challenge during development. Oxidation of Fc methionines is frequently observed, which leads to reduced affinity to FcRn and faster plasma clearance if present at high levels. A novel pH-gradient FcRn affinity chromatography method was developed to isolate antibody oxidation variants from an oxidized IgG1 preparation based on their FcRn binding properties. The subsequent physico-chemical and biological characterization of these oxidation variants demonstrated the value of the new method to study structure-function relationships.

2:30 Developability Assessment and Formulations Optimization of Biologics Using Isothermal Chemical Denaturation (ICD)

Sponsored by UNCHAINED LABS

Richard K. Brown, Ph.D., Unchained Labs

Stability optimization and aggregation minimization are two of the most important hurdles in the development of biologics. ICD provides the most accurate way of measuring protein stability under different formulation conditions. ICD experiments performed at different protein conc. provide a quantitative assessment of protein aggregation in the native and denatured states. ICD is ideally suited to optimize the formulation of highly concentrated formulations, bispecific antibodies and antibody drug conjugates. In this talk, the fundamentals of ICD and its application to the evaluation of protein stability and optimization of formulation conditions will be discussed.

3rd Annual

Rapid Methods to Assess Quality & Stability of Biologics:

Improving Prediction and Screening

3:00 Sponsored Presentation *(Opportunity Available)*

3:15 Poster Highlight Presentation: Leveraging Automation in Development of High Concentration Protein Formulations

Aastha Puri, M.Sc., Associate Scientist II, Drug Product Science & Technology, Bristol-Myers Squibb

Formulation development of high concentration products, brings a unique set of challenges, including the potential for increased physical and chemical stability risks, as well as challenges related to handling of viscous material. This work demonstrates the utility of new automation technologies in proficiently executing experimental workflows on a viscous high concentration protein formulation and assisting a data-driven decision making process as part of a material sparing, multi-well screening methodology.

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

4:15 A Comparison of Biophysical Characterization Techniques in Predicting Drug Product Stability

Andrew Semple, Scientist, Sterile Product and Analytical Development, Merck & Co.

To predict stability behavior, solution-mediated interactions (Colloidal, self-association propensity) and key molecular characteristics of ten formulated protein-therapeutics were compared to their stability at accelerated (25C and 40C) and long-term storage conditions (2-8C) as measured by size exclusion chromatography. Our results show that colloidal stability, self-association propensity, and conformational characteristics (exposed Trp) provide reasonable prediction of accelerated stability, with limited predictive value at 2-8C stability. Other measurements (e.g., thermal unfolding temperature) did not show any correlation.

4:45 HDX-MS Sheds Mechanistic Insights on Mutation Induced Changes in Physical Stability of an IgG1 mAb Engineered For Extended Serum Half-Life

CASE STUDY *Ranajoy Majumdar, Ph.D., Research Scientist, Biophysical Characterization, Biopharmaceutical Research and Development, Eli Lilly and Company*

A triple mutation in the CH2 domain of an IgG1 mAb intended to increase *in vivo* half-life resulted in decreased physical stability. Although the mutation induced minimal differences in H/D exchange kinetics at the mutation sites and the FcRn binding epitopes, it increased the flexibility of an established aggregation hotspot in the CH2 domain. This case study reinforces our understanding of the correlations between mAb physical stability and its local flexibility.

5:15 Close of Conference

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

Protein Aggregation: Mechanism, Characterization and Consequences

* Separate registration required; click **here** for details

2nd Annual

Early Analytical Development for Biotherapeutics

Optimizing the Selection and Performance of Preclinical Analytical Studies

WEDNESDAY, AUGUST 5

7:00 am Registration and Morning Coffee

8:05 Chairperson's Remarks

Mario Hubert, Ph.D., Principal Scientist, Bristol-Myers Squibb

» 8:15 KEYNOTE PRESENTATION: Early Analytical Development of Biotherapeutics; Case Studies and Lessons Learned

CASE STUDY *Ivan Correia, Ph.D., Senior Principal Research Scientist; Head, Global Protein Sciences, AbbVie Bioresearch Center*

The pre-clinical effort to identify and advance therapeutic molecules is challenging as resources are scarce for enabling rapid first-in-human studies. High throughput automation, platform methods and adopting best practices are all important. However, a commitment to innovate is needed to rapidly advance therapeutic programs. This presentation will use case studies and lessons learned to illustrate how AbbVie is rapidly advancing best in class therapeutics for patients.

MOLECULAR ASSESSMENT AND EARLY STAGE ANALYTICAL STRATEGIES

9:00 Early Developability Screen of Therapeutic Antibody Candidates Using Taylor Dispersion Analysis and UV Area Imaging Detection

CASE STUDY *Alexandra Lavoisier, Scientist, Biologics Center, Novartis, Switzerland*

Therapeutic antibodies represent one of the fastest growing segments in the pharmaceutical market. Early quality control and risk assessment of their biophysical parameters help prevent failure in later stages of development, reducing costs and time consumption. We report on a novel micro-capillary-based instrument (Viscosizer) for measuring both the hydrodynamic radius and the absolute viscosity of antibodies based on Taylor dispersion analysis and UV area imaging using nanoliters of samples.

9:30 Biophysical Analysis of the Compatibility of Monoclonal Antibodies in Intravenous Infusion Solutions to Overcome Possible Adverse Effects During Clinical Practice

CASE STUDY *Haripada Maity, Ph.D., Research Advisor, Eli Lilly and Company*

Administration of therapeutic monoclonal antibodies through the intravenous route can involve dilution of drug product using intravenous infusion solutions such as saline or 5% dextrose. As a result, the original drug product is diluted with potential changes in physical and chemical stability of the API. This presentation will discuss structural characterization, protein-protein interaction, concentration dependent inverse correlation of aggregation, and methods to monitor time-dependent self-association in intravenous infusion solutions.

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

ASSAY DEVELOPMENT AND TROUBLESHOOTING

10:45 Strategies and Challenges for Early Bioassay Method Development and Specification Setting

CASE STUDY *Debra Meyer, Senior Principal Scientist, Analytical R&D, Pfizer*

Pfizer has a robust pipeline of biotherapeutics including multiple modalities. Supplying biologically relevant bioassays across a large portfolio requires an evolution of a strategic, resource-flexible approach. Case studies will be used to illustrate a strategy for staged method development that delivers fit-for-purpose bioassays for early product development. The challenges and issues setting percent relative potency specification ranges for qualified bioassays early in development (prior to ICH validation) will be emphasized.

11:15 Biophysical Assays for Study of Aggregation and Subvisible Particles

CASE STUDY *Mario Hubert, Ph.D., Principal Scientist, Bristol-Myers Squibb*

The presence of subvisible particles can have a critical impact on drug product efficacy and potentially induce immunogenicity. Strategies and health authority expectations for characterization of particles below 10 um are evolving. This talk describes high throughput assay development for subvisible particle concentration and characterization. Flow imaging technique, supported by fluorescence and Raman microscopy was used to develop the assay. A statistical model is used to evaluate assay precision and recommended minimum sample sizes.

11:45 Sponsored Presentation *(Opportunity Available)*

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

1:30 Session Break

EARLY ANALYTICAL DEVELOPMENT FOR NOVEL BIOTHERAPEUTICS AND BIOSIMILARS

1:55 Chairperson's Remarks

Haripada Maity, Ph.D., Research Advisor, Formulation Development, CMC Development, Eli Lilly and Company

2:00 Analytical Development for Knob-into-Hole Bispecific Antibodies

Hongbin Liu, Ph.D., Scientist, Protein Analytical Chemistry, Genentech

Bispecific antibodies have shown great promise to be versatile and effective biotherapeutics. However, manufacturing of large quantity bispecifics with consistent quality remains to be a challenge. This presentation will focus on the analytical methods for a major format, knob-into-hole bispecifics, in

Early Analytical Development for Biotherapeutics

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development at Genentech. Details on method development for analyzing unique impurities, as well as overall analytical strategy for characterization and control systems will be discussed.

2:30 Analytical Development for Cell-Based Therapeutics

CASE STUDY *Gautam Banik, Ph.D., Vice President, Cellerant Therapeutics*

CLT-008 is an off-the-shelf cellular product containing myeloid progenitor cells derived from adult hematopoietic stem cells that have the ability to mature into neutrophils *in vivo*. Cellerant is developing CLT-008 as a treatment for neutropenia caused by chemotherapy or radiation. CLT-008 is under evaluation in a Phase II clinical trial in AML patients receiving chemotherapy. This talk will discuss the development of CLT-008 with a focus on analytical techniques for lot release.

3:00 PEGylation of Antibody-Based Therapeutics with Reduced Serum Half-Lives

Nathan Brown, Ph.D., Senior Scientist, AbbVie Bioresearch Center

The influence of PEG conjugation on therapeutics above the renal clearance threshold is not well understood. We have pursued strategies for incorporating PEG onto engineered antibodies with diminished half-lives, including chemical conjugation to native, interchain disulfides as well as to engineered, unpaired thiol mutations. The engineered mutations and PEG attachments were evaluated for alterations to the protein's biophysical properties, conjugation efficiency and specificity, antigen affinity, and *in vivo* half-life.

3:30 Identification of Quality Attributes in Early Biosimilar Development

CASE STUDY *Tilen Praper, Department Head, Analytical Development, Sandoz, Slovenia*

Biosimilars are biologics approved via stringent regulatory pathways, following a loss of exclusivity of their originator reference products. The basis for approval is the demonstration of comparability; there must be no meaningful difference in efficacy, safety and overall quality between the biosimilar and the originator. To achieve this, it is essential to know the critical quality attributes of the molecule and to control them properly during the development and production.

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

PLENARY SESSION

4:45 Chairperson's Remarks

Sam Ellis, Vice President, Biochemist, Thomson Instrument Co.

» 4:50 PLENARY KEYNOTE PRESENTATION:
Meeting the Needs of Patients with Rare Diseases: Innovation in Product Development

Joanne T. Beck, Ph.D., Senior Vice President, Pharmaceutical Development, Shire Pharmaceuticals

At Shire, where the delivery of innovative medicines to patients with rare diseases and other specialty conditions is a fundamental component of the business model, creative solutions are critical to our success. Starting with the transition of drug candidates from discovery research to the clinic, followed by late phase development and eventually commercial product lifecycle management, scientists and engineers focus on both technology innovation and creative business approaches to deliver high quality therapies to the patients while decreasing development timelines and costs.

5:20 Interactive Panel Discussion: How to Innovate Product Development

- Technologies
- Strategies
- Cutting Costs
- Meeting needs
- Utilizing creativity
- Lessons Learned

Moderator: Sam Ellis, Vice President, Biochemist, Thomson Instrument Co.

Panelists:

Joanne T. Beck, Ph.D., Senior Vice President, Pharmaceutical Development, Shire Pharmaceuticals

Wayne Froland, Ph.D., Associate Vice President, Center for Biopharmaceutical Manufacturing Sciences, Merck Manufacturing Division

Stefan Schmidt, Ph.D., M.B.A., Vice President, Process Science & Production, Rentschler Biotechnologie GmbH

Haripada Maity, Ph.D., Research Advisor, Eli Lilly and Company

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

7:00 End of Day

THURSDAY, AUGUST 6

8:00 am Registration and Morning Coffee

DEVELOPMENT AND TROUBLESHOOTING OF CELL-BASED POTENCY ASSAYS

8:25 Chairperson's Remarks

Kathleen Shields, Senior Research Scientist, Pfizer

8:30 Development and Troubleshooting of Cell-Based Potency Assays to Demonstrate Drug Mechanism of Action

CASE STUDY *Peggy Criswell, Ph.D., Senior Scientist, Merck & Company*

For an immunomodulatory biological therapeutic, three potency assays were developed, a competitive binding ELISA, a cell-based competitive binding ELISA, and a functional cell-based assay, utilizing a co-culture system of human Jurkat T-cells expressing the target and ligand presenting APCs. Each assay was implemented in the contract lab in parallel and validated or qualified. A case study is presented for assay implementation for product release and/or process characterization for licensure.

2nd Annual

Early Analytical Development for Biotherapeutics

Optimizing the Selection and Performance of Preclinical Analytical Studies

9:00 Method Development Guidance to Reduce Variability in Complex Cell-Based Potency Assays

CASE STUDY *Kathleen Shields, Senior Research Scientist, Pfizer*

Development of mechanistically relevant biological assays necessitates the execution of well-planned experiments. Accelerated drug development timelines and regulatory expectations for early introduction of functional bioassays in specific product categories (e.g. ADCs) challenge the method development scientist to efficiently optimize key assay parameters. A case study will be presented to illustrate the evaluation of assay parameters considered to be essential for delivery of a robust potency assay capable of supporting phase-appropriate specifications.

AUTOMATION AND EMERGING TECHNOLOGIES

9:30 Application of Differential Scanning Calorimetry in Biotherapeutic Comparability Analysis

William M. Matousek, Ph.D., Staff Scientist, Protein Biochemistry, Regeneron Pharmaceuticals, Inc.

Differential Scanning Calorimetry (DSC) is a sensitive technique commonly used to define protein thermal unfolding transitions, assess relative thermal stability, and compare higher order structural content. Multiple characteristic unfolding transitions are often observed, making the method amenable for both establishing identity and the estimation of impurities. Thermodynamic properties such as Tm, enthalpy, and heat capacity were evaluated as indicators of structural similarity and purity.

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

10:45 A High-Throughput Capillary Isoelectric Focusing Immunoassay for Protein Sialylation Fingerprinting

CASE STUDY *Lam Raga Anggara Markely, Ph.D., Scientist, Biogen Idec*

We developed a high-throughput method for semi-quantitative fingerprinting of protein sialylation using cIEF-immunoassay. The method is specific, sensitive, precise, and robust. It can analyze 2 µL unpurified cell culture samples within 4 hours (8 samples) to 14 hours (96 samples) without analyst supervision. It can be used for initial screening in cell line and process development, based on which a subset of samples can be further characterized by elaborate assays, such as LC and MS.

11:15 Fully Automated Host Cell Protein (HCP) Analysis using the AlphaLISA Assay for High Throughput Process Development

CASE STUDY *Zheng Ouyang, Automation Specialist, Biologics Process Development, Bristol-Myers Squibb*

An HCP AlphaLISA was fully automated and developed to enable "best in class" HTPD program development. The improvements introduced by this accomplishment include a cost reduction of 600% as compared to the traditional approach at improved sample throughput, and provided reliable insight into the HCP impurity reduction capability and robustness. This high-throughput assay capability is instrumental to support HT process development and to meet the Fast-to-FIH timelines.

11:45 Application of High Throughput Analytical Methods and Instrumentation

CASE STUDY *Ling Santora, Ph.D., Senior Scientist, AbbVie Bioresearch Center*

Success of a drug discovery and development campaign depends on the adequate supply and quality of targets and other protein reagents. Scarce resources and aggressive development timelines demand the need for reliable methods to rapidly screen and select for these reagents. At AbbVie we have developed various high throughput (HT) automated multi-dimensional HPLC platforms to purify and assess the quality of protein reagents to support early target discovery and cell line development. This talk will highlight these methods.

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

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

1:15 Close of Conference

Inaugural

Virus Detection, Clearance and Safety of Biologics:

Adventitious Agent Contamination, Risk Mitigation, New Technologies and Case Studies

THURSDAY, AUGUST 6

VIRAL SAFETY, RISK ASSESSMENT AND MANAGEMENT

1:55 pm Chairperson's Remarks

Horst Ruppach, Ph.D., Global Manager Viral Clearance and Global Coordinator Virology, Biologics Testing Solutions, Charles River Biopharmaceutical GmbH

» **KEYNOTE PRESENTATIONS:**

2:00 Application of Regulatory Guidance to New Molecular Detection Methods for Virology and Mycoplasmology

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

Molecular detection methods both old (PCR) and new including massively parallel sequencing, chip technology, and PCR combined with MASS Spec Time of Flight are ready to replace some of the classical virology detection methods. This talk will outline a path forward that the biotechnology industry can follow to successfully accomplish this change. An example of this path that has yielded success for mycoplasma PCR replacement of a culture method will be provided.

2:45 Mitigating Viral Contamination in Vaccines and Biologics Manufacturing

CASE STUDY *Otmane Boussif, Ph.D., Director, Purification & Formulation Processes, Sanofi Pasteur*

Contaminations of mammalian cell culture bioreactors are still being reported. In order to prevent this threat, manufacturers developed several risk mitigation strategies. Raw materials, media and solutions are the most likely source of contamination of mammalian cell-based operations, with risk related to material source and supply chain. Therefore implementations of additional point-of-use barriers risk, as well as sensitive analytical tools are considered. This presentation will discuss alternative technologies for media treatment through case studies.

3:15 Anion Exchange Membrane Adsorber and Viral Clearance Capacity – an Alternative to Anion Exchange Chromatography?

Horst Ruppach, Ph.D., Global Manager Viral Clearance and Global Coordinator Virology, Biologics Testing Solutions, Charles River Biopharmaceutical GmbH

Anion Exchange Chromotography shows frequently high viral removal capacity when run under certain conditions. This presentation will summarize experiences made with different types of Anion Exchange Membrane Adsorbers. The general capacity and robustness to remove viruses will be demonstrated and compared with the capacity of Anion Exchange Chromatography. The pros and cons of using Membrane adsorbers for viral clearance removal will be outlined and discussed based on experimental data.

3:45 Poster Highlight Presentation: Use of Virus Like Particle's as Viral Clearance Spiking Surrogates during Downstream Process Development Studies

David A. Cetlin, Founder & C.E.O., MockV Solutions LLC

Viral clearance studies are accomplished by challenging scaled-down versions of purification steps with live viral "spikes". These studies are typically conducted in BSL-2 facilities and are costly. A non-infectious viral surrogate would be useful for scientists developing or characterizing downstream purification process steps. Discussed here is an attempt to use a Virus Like Particle to determine the Mouse Minute Virus removal efficacy of a chromatography column step.

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

4:45 An Alternative Approach to Evaluation of Viral Clearance on New vs. End-of-Life Anion Exchange Chromatography Resin

CASE STUDY UNPUBLISHED DATA *William Daniels, MSc, Senior Scientist, Purification Process Development, Pfizer, Inc.*

A viral clearance study for new and used (end-of-life) anion exchange chromatography (AEX) resin evaluated the effect of extensive resin cycling on the capacity to bind virus in flow-through mode. A single column of new resin was tested alongside a single column of used resin, with both columns showing consistent capacity to clear two virus types in duplicate as well as demonstrating no viral particles in carryover ("mock") pools produced after each viral clearance run.

5:15 Panel Discussion: Advances in Viral Clearance and QbD Approach to Viral Safety

Moderator: Horst Ruppach, Ph.D., Global Manager Viral Clearance and Global Coordinator Virology, Biologics Testing Solutions, Charles River Biopharmaceutical GmbH

Panelists:

Paul W. Barone, Ph.D., Associate Director, Consortium on Adventitious Agent Contamination in Biomanufacturing, MIT Center for Biomedical Innovation

Otmane Boussif, Ph.D., Director, Purification & Formulation Processes, Sanofi Pasteur

Siemon Ng, Ph.D., Scientist, Microbiology & Virology Platform, Department of Analytical Research & Development North America, Sanofi Pasteur

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

5:45 End of Day

6:30-9:00 Recommended Dinner Short Course*

ABC: Anything But Chromatography – Precipitation, Crystallization and Flocculation

* Separate registration required; click here for details.

Inaugural

Virus Detection, Clearance and Safety of Biologics:

Adventitious Agent Contamination, Risk Mitigation, New Technologies and Case Studies

FRIDAY, AUGUST 7

8:00 am Registration and Morning Coffee

VIRAL CLEARANCE IN DOWNSTREAM PROCESSING & PURIFICATION

8:55 Chairperson's Remarks

Kathryn Martin Remington, Ph.D., Principal Scientist, Development Services, BioReliance

9:00 FEATURED PRESENTATION: A Survey of Industry Data on HTST, UV-C and Nanofiltration for Media Treatment and Their Efficacy of Removal and Inactivation of Virus

UNPUBLISHED DATA *Paul W. Barone, Ph.D., Associate Director, Paul W. Barone, Consortium on Adventitious Agent Contamination in Biomanufacturing (CAACB), MIT Center for Biomedical Innovation*

To reduce the risk of virus contamination in cell culture based biomanufacturing operations many manufacturers have implemented or begun to consider implementing large scale media treatment to remove or inactivate virus. Typical technologies that have been considered for this task are HTST treatment, UV-C irradiation and nanofiltration. CAACB consortium has collected member data and surveyed the literature to begin to assess the efficacy of each of these three media treatment technologies. A preliminary assessment of the results will be presented.

9:30 Successful Implementation of Modular Viral Clearance Claims for Early Phase Clinical Filings

CASE STUDY *Shilpa Ananthakrishnan, MSc, Scientist I, Process Sciences, Purification, AbbVie Bioresearch Center*

Demonstration of viral clearance capability is integral to developing downstream process. Dedicated viral clearance steps are incorporated into the process to ensure patient safety by providing robust and predictable capacity for virus removal and inactivation. In order to minimize viral clearance testing for early phase clinical programs, we have established modular claims for dedicated clearance steps within our platform manufacturing process. The claims have been successfully submitted in IND filings and have enabled greater efficiency in early and phase trials.

10:00 Coffee Break

10:45 Viral Risk Mitigation Strategies for Cell Culture Media and Other Raw Materials

UNPUBLISHED DATA *Kathryn Martin Remington, Ph.D., Principal Scientist, Development Services, BioReliance*

Contamination prevention strategies should involve a multi-faceted approach, including cell line screening, raw material testing and implementation of viral inactivation and removal steps in the downstream process. Other measures, such as viral reduction procedures for culture media and raw materials complement the strategy and may reduce the potential for viral contaminants to enter the downstream process. Data will be presented to demonstrate the efficacy of procedures such as UVC treatment and virus reduction filtration to reduce viruses in cell culture media.

11:15 Process Strategies to Improve Virus Clearance in Early Downstream Processing

CASE STUDY UNPUBLISHED DATA *Deqiang Yu, Ph.D., Senior Scientist, Process Development, Bristol-Myers Squibb Co.*

This talk will focus on virus clearance in early steps of downstream processing. Protein A step is used for virus clearance but not very effective. The strategies to improve virus clearance in Protein A will be discussed. Harvest treatment will be also discussed as a potential virus clearance step to increase process capability.

11:45 Extended Q&A with Session Speakers

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.

Sponsored by

12:15 Luncheon Presentation: Preventing Virus Contamination of Bioreactors with a Virus Barrier Filter

Christina Carbrello, Senior Scientist, EMD Millipore

Cell culture media is typically sterile filtered to remove bacteria and mycoplasma, however many bioreactors remain unprotected from viral contamination. Ideally, a filter could be used to remove viruses, but filtration is traditionally perceived as being unsuitable for the upstream processes. A new virus filter has been evaluated and demonstrated high levels of virus, bacteria and mycoplasma removal while providing high flow and capacity in chemically defined media with little to no impact on cell culture performance.

12:45 Session Break

TECHNOLOGIES FOR DETECTION OF NEW & EMERGING VIRUSES AND PATHOGENS

1:25 Chairperson's Remarks

Yoshifumi Hashimoto, Ph.D., Senior Scientist, Process Development, Protein Sciences Corporation

1:30 Implementation of an Adventitious Detection Assay Using High Throughput Sequencing within a Vaccine Manufacturer

Siemon Ng, Ph.D., Scientist, Microbiology & Virology Platform, Department of Analytical Research & Development North America, Sanofi Pasteur

NGS has great potential for testing cell substrates, raw materials, viral seed lots and crude harvests for adventitious agents. This technology has exquisite sensitivity and broad specificity. Implementing NGS can potentially streamline the adventitious testing package and replace animal testing. Data will be presented comparing the performance of NGS against qPCR and *in vitro* assay as well as the detecting adventitious agent in viral seed lots and other biological samples.

Inaugural

Virus Detection, Clearance and Safety of Biologics:

Adventitious Agent Contamination, Risk Mitigation, New Technologies and Case Studies

2:00 Next-Generation Sequencing Detection of Adventitious Agents

Brenda Richards, Staff Scientist, Functional Genomics, Genzyme, a Sanofi Company

Next-generation sequencing (NGS) is an emerging technology for pathogen detection in biopharmaceutical manufacturing allowing for the identification of both known and novel microorganisms. We have used this approach to confirm the identity of a causative agent in a bioreactor contamination and to establish the limits of detection for DNA and RNA viruses and bacteria in a background of Chinese hamster ovary cells. The presentation will include strategies, data, and conclusions from these experiments.

2:30 Incomplete Novel Sf9 Rhabdovirus is Detected in a Sf9 Cell Line

Yoshifumi Hashimoto, Ph.D., Senior Scientist, Process Development, Protein Sciences Corporation

A novel Sf9 rhabdovirus has been identified by next generation sequencing (NGS). We performed an analysis to verify Sf9 rhabdovirus RNA and searched for virus structures in cell culture supernatant. Our results showed an incomplete Sf rhabodovirus RNA containing a deletion of 320 nt of and absence of rhabodovirus-like particles in 1.14 g/ml fraction of the culture supernatant. We discuss discrepancy of data between NGS and conventional methods.

3:00 Networking Refreshment Break

SCALED-DOWN PROCESSES AS PREDICTIVE MODELS FOR LARGE SCALE PRODUCTION

3:15 Scaled-Down Model Qualification and Use for Process Improvement

Adam J. Meizinger, Ph.D., BS, Process Engineer II, Manufacturing Science and Technology Laboratory, Genzyme - a Sanofi Company

3:45 Challenges in Developing Predictive Downstream Scaled-Down Models

Omkar Joshi, Ph.D., Head, Downstream Development, Global Biologics, Bayer Healthcare

Scale-down models as appropriate representation of the manufacturing process are indispensable tools in characterization of biopharmaceutical manufacturing processes. During process development, such models enable evaluation of variability in input materials and parameters on a process and its impact on product quality to an extent that simply is not feasible at manufacturing scale. The key is to keep it simple and appropriate to needs. The presentation shows a pragmatic and systematic approach how to increase understanding of an antibody purification process by elements like scale-down modelling and qualification, cross-functional risk assessments, and process characterization studies.

4:15 Close of Conference

This Conference is also part of:
STREAM #5: Regulatory & Risk Management

Click here for details.

Cell Therapy Bioproduction:

Industrializing Cell Therapies

MONDAY, AUGUST 3

8:00 am Pre-Conference Registration and Morning Coffee

9:00-11:30 Recommended Short Course*
Analytical Strategies for Comparability in Bioprocess Development
* Separate registration required; click here for details.

11:30 Main Conference Registration

1:00 pm Chairperson's Opening Remarks
Anthony Davies, Ph.D., President, Dark Horse Consulting, Inc.

» 1:10 KEYNOTE PRESENTATION
I'm from the Government and I'm Here to Help - Navigating the Global Regulatory Maze for Cellular Therapeutics
Anthony Davies, Ph.D., President, Dark Horse Consulting, Inc.
The global regulatory framework for cell and gene therapies and regenerative medicine is in an era of rapid change and potential harmonization. This presentation will provide an up-to-the-minute road map of the path to approval for these drugs and their associated delivery devices.

COLD CHAIN, PROCUREMENT AND QUALIFICATION OF RAW MATERIALS & FINISHED PRODUCTS

1:45 Cold Chain Design for Allogeneic Cell Therapies
Brian Murphy, Ph.D., Director, Bioprocess Development, Celgene Cellular Therapies

2:15 Qualification of Raw and Ancillary Materials Used in Cell Therapy Manufacturing
Fouad Atouf, Ph.D., Director, Biologics & Biotechnology, U.S. Pharmacopeial Convention
Raw and ancillary materials are important components used in the manufacturing of cell- and tissue-based products. These materials can have a profound effect on the expansion, differentiation, or activity of the processed cellular components, and can therefore have a significant impact on the finished product quality attributes. Thus, ensuring the quality of a cell- or tissue-based therapeutic requires rigorous evaluation and qualification of the components used in its manufacture.

2:45 Refreshment Break

3:15 Sourcing and Qualification of Starting Materials for Cell Therapy Products
Elizabeth Read, M.D., Principal, EJ Read Consulting LLC.
The cellular starting material becomes an integral part of the living, functional cells that constitute the active drug substance of cell therapy products. This presentation will review the common types of cellular starting materials and cover approaches for their sourcing and qualification. Specific challenges in starting material qualification for patient-specific products (autologous or allogeneic) vs. off-the-shelf allogeneic products (multipotent or pluripotent stem cell-derived) will be addressed.

3:45 Raw Materials in the Manufacture of Advanced Therapies Medicinal Products: Quality Attributes and Quality Assurance
Bernd Leistler, Ph.D., Director, Development & Production, CellGenix GmbH
Regulatory agencies recognize an increasing need for guidance for raw materials used for ATMP production and started developing guidelines that outline risk-mitigation strategies and qualification programs for AM selection. AM manufacturers must ensure critical quality attributes to meet increasing quality and safety concerns. GMP grade and animal-derived component-free materials derived from well-characterized cell banks will reduce qualification and validation efforts of ATMP manufacturers and help to ensure consistency, safety and purity of the ATMP.

4:15 Breakout Discussions
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. Then continue the discussion as you head into the lively exhibit hall for information about the latest technologies.

Table: Chimeric Antigen Receptor (CAR)-T Cells: History, Success, Challenges and Advancement
Moderator: Pranay D. Khare, Ph.D., Independent Consultant
- CAR molecule development and advancement
- CAR-T cell manufacturing
- CAR-T cell safety and efficacy

Table: Hidden Challenges in Cell Therapy Processing
Moderator: Knut Niss, Ph.D., CMC Team Director, PO&T, Biogen

Table: Regulatory Pathways and Differences in US, Europe and Japan – Opportunities for Accelerating Development
Moderator: Anthony Davies, Ph.D., President, Dark Horse Consulting, Inc.

5:15 Discussion Report-Outs

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

7:00 End of Day

TUESDAY, AUGUST 4

7:30 am Registration and Morning Coffee

STRATEGIES FROM CLINIC TO COMMERCIALIZATION

7:55 Chairperson's Remarks
Pranay Khare, Ph.D., Independent Consultant

Cell Therapy Bioproduction:

Industrializing Cell Therapies

8:00 Translation of Cell-Based Gene Therapy Product into Clinical Phase II Trial

Ulrike Verzetnitsch, MSc, CTO, apceth GmbH

Treatment options based on genetically modified cells may add alternative therapeutic modalities to medical oncology. The in-house developed investigational medicinal product represented in this case study is a genetically modified mesenchymal-stem-cell-suspension (gmMSC) for IV infusion. The product for clinical Phase I was manufactured inhouse within the established GMP manufacturing capabilities. The Phase I study demonstrated the excellent tolerability of this first-in-man and first-in-class drug and data allowed for continuation in Phase II in Q1/2015.

8:30 Optimization and Clinical Manufacturing of Chimeric Antigen Receptor (CAR) T Cells for Solid Tumors

UNPUBLISHED DATA *Pranay D. Khare, Ph.D., Independent Consultant*

An optimal production process for the chimeric antigen receptor (CAR) expressing T cells (CAR-T) is required for their success in Adaptive T cell therapy clinical trials. Recently, outstanding results in several clinical trials with CAR-T in acute lymphoid leukemia (ALL) and chronic lymphoid leukemia (CLL]) has been achieved. But limited data and success is observed from solid tumors CAR-T clinical trials. This talk will focus on the optimization process and clinical manufacturing of CAR-T production process for solid tumors.

9:00 Stem Cell Therapy – The Road to Commercialization

Jasmin Kee, Ph.D., Head, Engineering, ReNeuron

Our lead product, CTX, is a therapy for the treatment of patients left disabled by a stroke and for critical limb ischaemia. Both treatments are currently in Phase I and II clinical trials. This presentation will discuss the challenges faced through clinical trials and the strategy to commercialization. Topics will include the use of contract manufacturers versus in-house manufacturing, process scale-up and the use of automation to meet clinical trial needs and future commercial supply.

9:30 Sponsored Presentation *(Opportunity Available)*

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

SCALING UP AND MANUFACTURING CHALLENGES

10:30 Overcoming Comparability and Scale-Up Challenges in Cell Therapy Production

Robert Deans, Ph.D., EVP, Regenerative Medicine, Athersys, Inc.

Advancing cell therapeutics to commercialization requires adapting early pilot scale clinical manufacturing to a scale meeting commercial expectations. Improvements and scaling cell processing can involve radical shifts in bioreactor format, often moving from 2D planar culturing to microcarrier based bioreactor formats. A case study will be presented for comparability analysis involving MultiStem®, an adherent adult stem cell product, in commercialization for cardiovascular and CNS indications.

11:00 Manufacturing Challenges and Solutions for Autologous Cell Therapies

Knut Niss, Ph.D., CMC Team Director, PO&T, Biogen

Compared to traditional drugs where a bulk of drug substance is produced and dispersed to several individual patients, autologous cell therapy products are derived from the patient's own cells. With this, a unique manufacturing scenario exists where each patient equals one manufacturing batch. Thus, the commercialization strategy for such products needs to consider several unique issues. This presentation will discuss these issues in detail in light of establishing a large market for an autologous therapy.

11:30 Cell Expansion and Scaling Up in 3D: Implementing an Optimized, Standardized and Fully Automated Operation

Ohad Karnieli, Ph.D., Vice President, Technology & Manufacturing, Pluristem Therapeutics

Technologies are evolving to allow production of cells in large quantities under GMP conditions, nevertheless, the advantage opens new questions and challenges including quality, identity, reproducibility and cost. Bioreactor technology brings to the industry the opportunity to manufacture large quantities of cells in a tightly controlled environment, lowering relatively the COGS and improving quality. However within it there are many unmet challenges. The talk will describe the main challenges and possible solutions for bioreactor 3D culturing.

12:00 pm Translating Cell Therapies: Academic vs. Industry Model

Alexey Bersenev, Ph.D., Director, Advanced Cell Therapy Lab, Yale University

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

1:15 Session Break

SCALING UP AND MANUFACTURING CHALLENGES (cont.)

1:55 Chairperson's Remarks

Robert Deans, Ph.D., EVP, Regenerative Medicine, Athersys, Inc.

2:00 Scalable, cGMP-Compliant Process for Autologous Cell Therapy Production and Scale-Up

Marty Giedlin, Ph.D., Executive Director, CMC, Novartis Pharmaceuticals Corp.

2:30 Development Strategies for kSep Single-Use Continuous Centrifuge Processes

CASE STUDY *Jonathan Rubin, Ph.D., Scientist, API Large Molecules, Janssen Pharmaceuticals*

Centrifugation is often employed during downstream processing to clarify or concentrate biologics (e.g. antibodies, vaccines, and cell therapies). Disposable centrifuge technology has greatly reduced preparation/cleaning time and contamination risk. Generally, cell therapy products are concentrated in the centrifuge (retentate), whereas clarified vaccine and antibody products flowthrough the centrifuge (centrate). This talk will give a basic overview of kSep technology and discuss strategies used to develop processes for cell therapy and vaccine products

Cell Therapy Bioproduction:

Industrializing Cell Therapies

3:00 Perfused Bioreactor for the Optimization of Human Stem Cell Culture

Veronique Chotteau, Ph.D., Principal Investigator, Cell Technology Group, School of Biotechnology, KTH, Royal Institute of Technology

We have created small perfusion bioreactors supporting the culture of human stem cells adhering on electrospun nanofiber scaffold of biocompatible and biodegradable polymer in EU project HESUB. The bioreactors are scale-down of a novel 50 mL perfusion bioreactor and are used to develop and optimize perfusion processes of human stem cells. We will review our achievements for the culture of human myogenic progenitors and of human pluripotent stem cells, embryonic and induced.

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

TOOLS AND TECHNOLOGIES TO ENHANCE CELL CULTURE PROCESSES

4:15 Biologics Data Platform for Tailored Support of Cell Line Development

Christian Bender, Ph.D., Computational Biologist, Global Drug Discovery, Global Biologics, Bayer HealthCare

We have successfully implemented the Biologics Data Platform (BDP) for tailored support of our screening and protein production processes. In the context of our cell line development process, we present the integration of BDP with our automation workstation. We demonstrate the power of using a comprehensive data management platform to track data for cell line clones and fed-batch experiments together with molecule information such as primary sequences and experimental results.

4:45 Portable X-Ray Fluorescence Spectrometer: A Tool for Biopharmaceutical Forensic Investigations

Jessica Mondia, Ph.D., Research Scientist, Biogen Idec, Inc.

A portable X-ray fluorescence (XRF) spectrometer is a small, cheap, easy and fast instrument for multi-elemental analysis. In biopharma, forensic investigations usually refer to determining the root-cause and evaluating the risks associated with deviations from GMP guidelines including batch records, procedures and SOPs. Here we introduce the use of a XRF spectrometer for biopharmaceutical forensic applications as an in-house-portable diagnostic tool to help resolve or guide investigations in a timely fashion.

5:15 Close of Conference

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

Incorporating the Concepts of Pharmaceutical Quality Systems into Cell Therapy Products

* Separate registration required; click here for details.

Inaugural

Continuous Processing in Biopharm Manufacturing

Economics, Regulatory, Integration and Practical Implementation

WEDNESDAY, AUGUST 5

7:00 am Registration and Morning Coffee

CONTINUOUS PROCESSING AS A DISRUPTIVE INNOVATION IN BIOPROCESSING

8:05 Chairperson's Remarks
Massimo Morbidelli, Ph.D., Professor, Institute for Chemical and Bioengineering, Department of Chemistry and Applied Biosciences, ETH Zürich

» 8:15 KEYNOTE PRESENTATION: Continuous Processing – Rewrite of the Rules?
Wayne Froland, Ph.D., Associate Vice President, Center for Biopharmaceutical Manufacturing Sciences, Merck Manufacturing Division

9:00 The Future State of Bioprocessing
Lawrence Weiner, Senior Director, Strategic Innovation, Biogen Idec
Disruptive innovation is required to deliver game changing improvements demanded by the market and industry. We will discuss Biogen's approach to implementing near term sustaining and long term disruptive technologies. The discussion will include how technologies are selected and driven forward to implementation. We will also discuss a few opportunities for innovation within existing technologies and share thoughts on continuous manufacturing as an alternate route to maximize productivity.

9:30 The Old Is New Again: A Fair and Balanced Assessment of Continuous Bioprocessing
Sadettin S. Ozturk, Ph.D., Assoc Deputy Director, Process & Analytical Development, MassBiologics
Although it is somehow branded as new, continuous bioprocessing has been utilized over 25 years that has resulted in more than 15 licensed biopharmaceuticals. Recent attempts of re-popularizing the continuous bioprocessing receive mixed reactions form the industry: great enthusiasm, confusion, and skepticism. This talk will present an assessment of continuous bioprocessing against well-established fed-batch platform and provide a historical and futuristic perspective.

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

CONTINUOUS PROCESSING VS. FED-BATCH: ECONOMIC AND REGULATORY PERSPECTIVES

10:45 Economics of Continuous Processing Vs. Traditional Batch
Jeff Johnson, New Technology Lead, Merck & Co. Inc.
Opportunities for applying new technologies integrated with continuous processing and enabled by single use will be discussed for monoclonal antibody production. The combined efficiencies gained by continuous processing will be compared by economic criteria to current manufacturing methods. In addition the impact of the new approaches to multi product manufacturing facilities will be described.

11:15 The Regulatory and Quality Perspective on Continuous Processing
Robert Kozak, Ph.D., Senior Regulatory Science Advisor, Global Regulatory Affairs, Bayer Healthcare
Continuous perfusion production has enabled flexible manufacturing of rFVIII, a large complex biotech product, for over two decades. Continuous improvement has driven frequent process, equipment and facility changes supported by comparability exercises assessing the impact to quality product attributes throughout the entire fermentation campaign which can be months in duration. Examples of process changes implemented and non-implemented will be reviewed along with the impact of a changing regulatory environment.

11:45 Simplifying Continuous Chromatography Process Development - Optimisation Parameters to Fit Business Need
Sponsored by PALL Life Sciences
René Gantier, Ph.D., R&D Director, Biopharm Applications, Pall Life Sciences
Continuous capture multicolumn chromatography (MCC) is a key unit operation in the development of continuous, integrated processes. But how are continuous capture MCC processes developed and optimized using only small quantities of feedstock? We have developed and tested a new method to accurately translate data from a minimal number of single column runs into a low cost multicolumn process. This new simple process transfer from batch to continuous enables process optimization to fit business needs.

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

1:30 Session Break

INTEGRATION OF UP- AND DOWN-STREAM PROCESSING

1:55 Chairperson's Remarks
Andrew Sinclair, FREng, MSc, President & Founder, Biopharm Services Ltd.

2:00 Integration of Up- and Downstream Continuous Processing
Massimo Morbidelli, Ph.D., Professor, Institute for Chemical and Bioengineering, Department of Chemistry and Applied Biosciences, ETH Zürich
We discuss here a series of experiments where a perfusion reactor with CHO cells for the production of a monoclonal antibody has been operated in the continuous mode and connected to a two column continuous protein A chromatographic unit for product capture. A few steady states are examined and the use of simulation models for process design and control is illustrated.

2:30 Continuous Manufacturing: Upstream vs. Downstream Issues and the Drivers
Andrew Sinclair, FREng, MSc, President & Founder, Biopharm Services Ltd.
Our experience of modelling continuous bioprocess operations allow us to provide insights into the status of continuous bioprocessing. This allows us to identify those factors that require optimization/

Inaugural

Continuous Processing in Biopharm Manufacturing

Economics, Regulatory, Integration and Practical Implementation

development and to understand the potential now and for the future. In particular we focus on the influence of upstream versus downstream and the implication of technology trends on the value proposition for continuous operation.

3:00 Continuous Operations in Biopharm Manufacturing: Back to the Future

UNPUBLISHED DATA *Jean-Marc Bielser, Scientist, BioProcess Science, Merck Serono*

At early stage of bioprocess science, continuous operations were the workhorse in the industry. Then, for the past 10 years, we moved towards fed-batch operations. Recently, continuous operations is considered again as a lever to boost process productivity and control product quality. Looking at bioprocess history, this presentation will discuss the reasons of those "back and forth" trends. It will also present results obtained at EMD-Serono using continuous operations in cell-culture and also in purification of biopharmaceuticals. Finally, it will discuss the challenges and opportunities of continuous operations versus current established fed-batch platform.

3:30 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 explore potential solutions to persistent challenges.

Table: Perfusion processes have several advantages, which make them perceived as possible solutions for the future. What are the impediments for perfusion process expansion today and how should we tackle these?

Moderator:

Veronique Chotteau, Ph.D., Principal Investigator, Cell Technology Group, School of Biotechnology, KTH, Royal Institute of Technology

Table: An Examination of Barriers to the Commercial Adoption of Continuous Processes for Production of Biologicals

Todd Przybycien, Ph.D., Professor, Chemical Engineering and Biomedical Engineering, Carnegie Mellon University

Table: The Challenges of Keeping Pharmaceutical Aging Facilities Fit for Purpose

Moderator: Morten Munk, Senior Technology Partner, Global Business Development, NNE PharmaPlan

Aging facilities are a major concern for industry and regulators, due to the risk of supply of suboptimal quality products and possibly drug shortage situations. Join this roundtable discussion to share insight on the challenges and what might hold the industry back from implementing up-to-date solutions. The focus will not only be around the facilities, but also the processes, analytical methods and manufacturing control strategies, and with special focus on the regulatory impact and strategy for implementing the needed changes in all the mentioned areas.

Table: Implementing Continuous Bioprocesses in GMP Manufacture

Moderator: Peter R. Levison, Ph.D., Senior Marketing Director, Downstream Processing, Pall Life Sciences

- Assuming the purification technologies and materials used in both batch and continuous processes are identical are these processes interchangeable during design, development, scale-up and production?
- Large fed batch culture is today's start point for DSP. Does the future include a series of staged smaller fed batch bioreactors and/or perfusion cell culture processes
- What other platforms and/or continuous processes are required for non-Mab applications?

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

PLENARY SESSION

4:45 Chairperson's Remarks

Sam Ellis, Vice President, Biochemist, Thomson Instrument Co.

» 4:50 PLENARY KEYNOTE PRESENTATION: Meeting the Needs of Patients with Rare Diseases: Innovation in Product Development

Joanne T. Beck, Ph.D., Senior Vice President, Pharmaceutical Development, Shire Pharmaceuticals

At Shire, where the delivery of innovative medicines to patients with rare diseases and other specialty conditions is a fundamental component of the business model, creative solutions are critical to our success. Starting with the transition of drug candidates from discovery research to the clinic, followed by late phase development and eventually commercial product lifecycle management, scientists and engineers focus on both technology innovation and creative business approaches to deliver high quality therapies to the patients while decreasing development timelines and costs.

5:20 Interactive Panel Discussion: How to Innovate Product Development

- Technologies
- Strategies
- Cutting Costs
- Meeting needs
- Utilizing creativity
- Lessons Learned

Moderator: Sam Ellis, Vice President, Biochemist, Thomson Instrument Co.

COMPANION CONFERENCE:
Advances in Purification Technologies (August 6-7) – click **here** for details

Inaugural

Continuous Processing in Biopharm Manufacturing

Economics, Regulatory, Integration and Practical Implementation

Panelists:
Joanne T. Beck, Ph.D., Senior Vice President, Pharmaceutical Development, Shire Pharmaceuticals
Wayne Froland, Ph.D., Associate Vice President, Center for Biopharmaceutical Manufacturing Sciences, Merck Manufacturing Division
Stefan Schmidt, Ph.D., M.B.A., Vice President, Process Science & Production, Rentschler Biotechnologie GmbH
Haripada Maity, Ph.D., Research Advisor, Eli Lilly and Company

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

7:00 End of Day

THURSDAY, AUGUST 6

8:00 am Registration and Morning Coffee

IMPLEMENTATION CHALLENGES IN UPSTREAM PERFUSION AND DOWNSTREAM CHROMATOGRAPHY

8:25 Chairperson's Remarks
Andrew Zydney, Ph.D., Distinguished Professor, Chemical Engineering, The Pennsylvania State University

8:30 Perfusion Process for Very High Cell Density of CHO Cells
Veronique Chotteau, Ph.D., Principal Investigator, Cell Technology Group, School of Biotechnology, KTH, Royal Institute of Technology
Perfusion processes at high cell densities are perceived as a viable solution for the production of biopharmaceuticals, allying small volume bioreactors, compatibility with disposable equipment and continuous manufacturing concept reclaimed by the Health Authorities. We will review our strategy for the development of high cell density processes looking in particular at the medium renewal rate minimization using cell separation by Alternating Tangential Flow filtration.

9:00 Continuous Chromatography – Why, When and How?
UNPUBLISHED DATA *Andrew Zydney, Ph.D., Distinguished Professor, Chemical Engineering, The Pennsylvania State University*
There is growing interest in the use of continuous unit operations for bioprocessing with the ultimate goal of developing an integrated continuous process. This talk will focus on the opportunities for continuous chromatographic separations, including both the challenges and the potential advantages of this approach. Specific examples will be shown for the application of periodic (multi-column), simulated moving bed, and countercurrent tangential flow chromatography to the purification of monoclonal antibodies.

9:30 Continuous Multi-Column and Integrated Purification Strategies for Enveloped Virus-Like Particles and Non-Enveloped Viruses
Ricardo Silva, Ph.D., Downstream Processing Research, iBET - Instituto de Biologia Experimental e Tecnológica
The growing interest on enveloped virus-like particles and non-enveloped viruses for vaccines and gene therapy applications led to the development of new purification strategies capable of coping with the challenges presented by these new products. Innovation in downstream processing should therefore aim not only at productivity increase but also at process economy whilst complying with regulatory requirements. Evaluation of integrated purification strategies and two-column semi-continuous chromatographic systems for virus and enveloped virus-like particles will be reported. Significant improvements in yield and product quality thus obtained will be highlighted.

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

10:45 A Continuous Precipitation Process for High-Titer Recombinant Protein Capture and Purification
UNPUBLISHED DATA *Todd Przybycien, Ph.D., Professor, Chemical Engineering and Biomedical Engineering, Carnegie Mellon University*
Coupled precipitation-filtration operations can form the basis of a continuous, scalable, economical and generalizable platform process for the primary recovery of high titer recombinant proteins. We have used synergistic combinations of precipitants to selectively precipitate target proteins, spanning a broad range of physical properties, against backgrounds of complex contaminants. We have evaluated the performance of the proposed process with simulations and reduced it to practice with an industrial partner.

11:15 Behavior of a Ceramic Membrane-Based Perfusion CHO Culture System for Production of IgG1
Jean-Francois Hamel, Ph.D., BPEC Core Laboratory Supervisor, MIT

11:45 Continuous Chromatography in Downstream Processing – How to Make It a Reality
Kathleen Mihlbachler, Ph.D., Global Director, Separations Development, LEWA Process Technologies
Multi-column continuous chromatography has recently become an enabling technology that will "break the bottleneck" in downstream processing of biopharmaceuticals. Continuous chromatography has shown promises in reduction of manufacturing cost. However, up to today there has not been a reported case at the production scale. What are the remaining technical barriers when implementing the technology in the GMP environment? This presentation highlights how to overcome the major barriers when developing this technology platform.

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12:15 pm What is Holding the Industry back from Implementing Continuous Processing More Broadly?

Morten Munk, Ph.D., Senior Technology Partner, Global Business Development, NNE PharmaPlan

Based on a survey among industry peers on continuous processing, this presentation will address various concerns around continuous processing, and real concerns are distinguished from perceived concerns. This presentation will not be another presentation on the financial benefits of continuous processing or a report on the newest equipment on the market. The aim of the presentation is to discuss and illustrate other elements which make the difference between success and failure when a continuous processing strategy is evaluated and implemented.

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

1:15 Close of Conference

Inaugural

Bioprocess Quality and Regulatory Compliance

A best practices forum for process characterization, control strategies and maintaining quality throughout the product lifecycle

MONDAY, AUGUST 3

8:00 am Pre-Conference Registration and Morning Coffee

9:00-11:30 Recommended Short Course*
Optimizing Media – Achieving Super Soup
* Separate registration required; click here for details.

11:30 Main Conference Registration

1:00 pm Chairperson's Opening Remarks
Bob Kozak, Ph.D., Senior Regulatory Science Advisor, Bayer HealthCare Pharmaceuticals

» 1:10 KEYNOTE PRESENTATION: Analytical Methods and Specification Revisions during the Product Lifecycle
CASE STUDY *Stephan O. Krause, Ph.D., Director, QA Technical Support, AstraZeneca Biologics*
This presentation provides best practices for specifications setting for clinical biological products within the framework of ICH guidelines on pharmaceutical development (Q8(R2) and Q11), quality risk management (Q9) and quality systems (Q10). The need to link the life cycles of test method(s) and specifications is illustrated. A case study illustrates how the IMP specification revision process can be managed and how specifications can be set and justified for early and late development stages.

RISK ASSESSMENT AND REGULATORY COMPLIANCE

1:45 Strategies for Immunogenicity Risk Assessment and Regulatory Compliance
Bob Kozak, Ph.D., Senior Regulatory Science Advisor, Bayer HealthCare Pharmaceuticals
Many biotherapeutic products are immunogenic with minimal tools for predicting clinical outcome, therefore immunogenicity risk identification, analysis, evaluation, mitigation and management need to be incorporated into your programs as an iterative process. Immunogenicity risk assessment strategy, process and regulatory expectations will be discussed.

2:15 Implementation of QbD Principles into Commercial Process Development and Process Characterization for mAbs and Fc-fusion Proteins
CASE STUDY *Angela Lewandowski, Ph.D., Manager, Biologics Process Development, Bristol-Myers Squibb*
Risk assessments are a useful tool during commercial process development and process characterization to drive process control strategies, thereby ensuring consistent process performance and product quality. This talk will focus on the implementation of QbD principles (via risk assessment and management) during upstream and downstream commercial process development and characterization. Case studies for both mAbs and Fc-fusion proteins will be discussed.

2:45 Refreshment Break

3:15 Risk Management of Regulatory Submissions
James Stonecypher, Regulatory Affairs Executive
Identifying and managing risks is an essential and continuous activity in the development of (bio) pharmaceutical products. ICH Guideline Q9 outlines the principles, process, and tools for utilizing quality risk management in the pharmaceutical industry. Risk management activities are often overlooked or underutilized in the regulatory submissions process. This presentation will discuss the benefits and applications of risk management for regulatory submissions and practical examples of how it can be implemented.

3:45 Regulatory Issues in the Development of a Biosimilar Rituximab
CASE STUDY *Mauricio Seigelchifer, Ph.D., Director, Tech Transfer, Mabxience, Argentina*
The development pathway for biosimilar medicines is established in guidelines from WHO, EMA and more recently FDA and different Latin American countries. The process, from the cloning, passing through upstream and downstream, has to be driven to obtain a highly similar molecule to the reference product. Here we present a case study of a biosimilar Rituximab developed and produced to fulfill these biosimilar requirements. We also present the comparison with the market reference.

4:15 Breakout Discussions
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. Then continue the discussion as you head into the lively exhibit hall for information about the latest technologies.

5:15 Discussion Report-Outs

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

7:00 End of Day

TUESDAY, AUGUST 4

7:30 am Registration and Morning Coffee

PROCESS CHARACTERIZATION AND IDENTIFICATION OF CRITICAL PROCESS PARAMETERS

7:55 Chairperson's Remarks
Karthik P. Jayapal, Ph.D., Deputy Director, Manufacturing Technologies, Sanofi-Pasteur

Inaugural

Bioprocess Quality and Regulatory Compliance

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8:00 Challenges and Learnings Applying Retrospective QbD for Marketed Biologics

Kenneth Green, Ph.D., Head, Manufacturing Science and Technology, Shire

For clinical candidates, QbD is generally applied during development and commercialization phases as a standardized business process. However, this is not typically the case for marketed products where retrospective QbD requires consideration of established controls and regulatory commitments. This talk discusses Shire's approach for retrospective QbD for marketed products including establishing a business process, associated criticality and change control strategy via application of risk assessments, and the behavioral changes required for successful implementation.

8:30 Product Characterization Methods and Strategies for Process Development

CASE STUDY *Christine P. Chan, Ph.D., Principal Scientist and Technical Lead, Manufacturing Science & Technology, Genzyme - a SANOFI company*

Development of complex glycoproteins requires an array of analytical techniques to adequately understand and control product quality during the manufacturing process. This presentation will discuss strategies in product testing and review case studies on characterization of different proteins in support of process development.

9:00 Troubleshooting Bacterial Vaccine Production

CASE STUDY *Karthik P. Jayapal, Ph.D., Deputy Director, Manufacturing Technologies, Sanofi-Pasteur*

The use of complex raw materials like casamino acids or soy hydrolysates in bacterial fermentation can contribute to process and ultimately product variability. This case study will focus on our approach to mitigating such risks for a bacterial vaccine production process by exploring opportunities for better raw material characterization, improved process robustness and simplifying, and/or modernizing the current manufacturing process.

9:30 Sponsored Presentation *(Opportunity Available)*

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

10:30 Using New Analytical Technologies for Process Characterization

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

Initiatives such as PAT and QbD, plus the desire to continuously improve production by leveraging process comparability paradigms, have enhanced the need to utilize both classic and state-of-the-art analytics for upstream and downstream characterization and comparability exercises. This talk will provide an overview of current applications of analytics in process development, and highlight practical issues to be considered in selecting and applying a wide array of analytical technologies to biotechnology processes.

11:00 Analytical Characterization to Support Development of Antibody Biopharmaceuticals: Identity, Purity, Potency and Safety

CASE STUDY *Xuan Gao, Ph.D., Scientist, Sutro Biopharma, Inc.*

During our early development of an IgG1 molecule, LC/MS/MS was used to identify sequence variants and post translational modifications; Biacore and other assays were used to determine consequences of such variants and modifications on potency and safety. We correlated characterization results with process procedures to identify the root cause of sequence variants and modifications. Furthermore, rapid analytical methods were developed to support screening and production of desired molecule during development.

11:30 Bioprocess Characterization Approach for a Marketed Biosimilar

CASE STUDY *Daliborka Dušanić Ph.D., Validation Lead, MS&T, Lek Pharmaceuticals, Slovenia*

For the registration of legacy products marketed outside the US, FDA regulations demanding in depth understanding of sources of variability in the production of a biosimilar can be challenging. The knowledge gained during process characterization can be beneficial from the manufacturing and QA perspective; however, it can also pose business risks such as the need for re-validation and changes in filings in other countries. This case study reviews the approach for PC of a legacy biosimilar product.

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

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

1:15 Session Break

CONTROL STRATEGIES AND ONLINE PROCESS MONITORING

1:55 Chairperson's Remarks

Zhimei Du, Ph.D., Principal Scientist, Teva Pharmaceuticals

2:00 Utilization of Advanced Process Control to Drive Consistent Processes in Mammalian Cell Culture

Vijay Janakiraman, Ph.D., Senior Engineer, Biogen Idec

Advances in online process monitoring have paved the way for the next generation of control strategies for achieving advanced process control. The end result will be more consistent process performance and product quality control. This talk will provide insight into new process analytical technologies (PAT), such as spectroscopy and biocapacitance, to assist in the implementation of online process monitoring.

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Bioprocess Quality and Regulatory Compliance

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2:30 Control Strategy Approach for a Well-Characterized Vaccine

CASE STUDY *Parag Kolhe, Ph.D., Senior Principal Scientist, Pfizer*

Robust control strategy as proposed in ICH Q10 is the foundation for ensuring consistent process performance and product quality. This presentation will describe approach towards developing control strategy during development lifecycle. Case study will be presented for well-characterized vaccine product that illustrates the approach and its utility during process performance qualification (PPQ) and commercial manufacturing.

3:00 Practical Considerations of Using Real-Time Multivariate Statistical Process Monitoring to Ensure Batch Consistency

CASE STUDY *Eric Kwei, Process Engineer, Amgen*

Commercial bioprocess manufacturing facilities generate significant amounts of continuous data that can be challenging to analyze effectively. Presenting meaningful, accessible, and timely conclusions about this data requires a broad understanding of statistical methodology, process design, process automation, and human factors. The intersection of these elements will be discussed in the context of a real-time multivariate process monitoring program implementation.

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

4:15 Deciphering Factors that Have Impacts on Glycosylation of mAb and its Biophysical Properties

Zhimei Du, Ph.D., Principal Scientist, Teva Pharmaceuticals

Consistent and reproducible generation of mAb glycoform profiles still remains a considerable challenge in biopharmaceutical industry. To assess the mechanism of immature glycan process, and to minimize the environment-mediated lot-to-lot variations, we identified a broad range of factors that impact on the glycosylation maturation of mAbs. Our results indicate that high mannose may lead to changes in biophysical properties including protein conformation, thermal stability, colloidal stability, and aggregation propensity.

4:45 Core Components for Contamination Prevention and Control in Biopharmaceutical Manufacturing Operations

Gary C. du Moulin, Ph.D., M.P.H, RAC, Adjunct Associate Professor of Drug Regulatory Affairs, Massachusetts College of Pharmacy and Health Sciences University

Microbial contamination in bioprocessing operations remains a key concern in plant operations. Microorganisms, such as Acinetobacter baumanii, find areas in our manufacturing facilities to reside and constitute a potential risk to bioreactor operations. Contamination events result in costly delays and restarts but most importantly, threaten the supply of lifesaving products to our patients. This presentation identifies those core components of contamination prevention which if implemented can provide the greatest impact in minimizing the microbiological risks in our manufacturing sites.

5:15 Close of Conference

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

Patent Strategies for Bioprocess Scientists

* Separate registration required; click here for details

COMPANION TRAINING SEMINAR AND CONFERENCE:

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Conference Venue and Hotel:

Westin Copley Place
10 Huntington Ave.
Boston, MA 02216
Phone: 617-262-9600

Discounted Room Rate: $259 s/d
Discounted Cut-off Date: July 7, 2015

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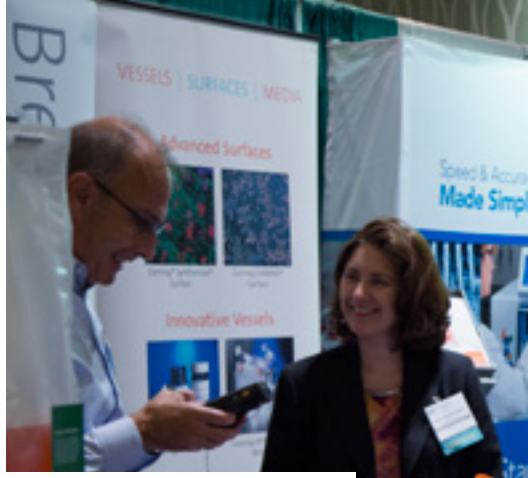

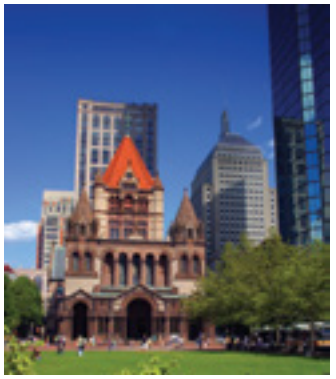

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