Cambridge Healthtech Institute's 13th Annual

PEPTALK
The Protein Science Week

January 13-17, 2014
Renaissance Hotel and Palm Springs Convention Center, Palm Springs, California

Register by September 13
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Pipeline 5: Expression and Production
Sixth Annual
Engineering Genes, Vectors, Constructs and Clones
Sixteenth Annual
Recombinant Protein Expression and Production
Inaugural
Transient Protein Production

Pipeline 6: Purification and Aggregation
Sixth Annual
Protein Purification and Recovery
Third Annual
Higher-Throughput Protein Purification
Fifth Annual
Protein Aggregation and Emerging Analytical Tools

Pipeline 7: Manufacturing and Facilities
Inaugural
Single-Use Technologies and Continuous Processing
Inaugural
Flexible Manufacturing of Biopharmaceuticals
Second Annual
Extractables and Leachables

Organized by Cambridge Healthtech Institute
CHI-PepTalk.com

KEYNOTE SPEAKERS

Lorenz M. Mayr, Ph.D.
Vice President, Reagents & Assay Development, AstraZeneca, Inc.

Sabine Geisse, Ph.D.
Director/NLS, Novartis Institutes for BioMedical Research

Yan-ping Yang, Ph.D.
Director, Downstream Purification, Bioprocess Research & Development, Sanofi Pasteur

Ian Hunt, Ph.D.
Group Leader, Protein Sciences, Novartis

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

Jerold Martin
MSc, Chairman, BPSA BoD and Technology (E+L) Committee

Sadettin S. Ozturk, Ph.D.
Head, Process and Analytical Development, MassBiologics

Desmond G. Hunt, Ph.D.
Senior Scientific Liaison, US Pharmacopoeial Convention, USP

Dennis Jenke, Ph.D.
Baxter Distinguished Scientist, Technology Resources, Baxter Healthcare Corp.

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Hotel & Travel Information

**Conference Venue:**
Palm Springs Convention Center  
277 N. Avenida Caballeros  
Palm Springs, CA 92262

**Host Hotel:**  
Renaissance Palm Springs Hotel  
888 E. Tahquitz Canyon Way  
Palm Springs, CA 92262  
Phone: 760-322-6000

**Discounted Room Rate:** $195 s/d  
**Discounted Room Rate Cut-off Date:** December 12, 2013

Please visit CHI-PepTalk.com to make your reservations online or call the hotel directly to reserve your sleeping accommodations. You will need to identify yourself as a Cambridge Healthtech Institute conference attendee to receive the discounted room rate with the host hotel. Reservations made after the cut-off date or after the group room block has been filled (whichever comes first) will be accepted on a space- and rate-availability basis. Rooms are limited, so please book early.

**Please visit our website for Airline and Car Rental discounts.**

**Hotel-Airport Shuttle Service:** The Renaissance Hotel is pleased to offer a complimentary shuttle service from the airport to the hotel. To make use of this service, please first collect your luggage and then proceed to the courtesy phone located in the baggage claim area. After notifying the hotel, the shuttle will arrive in approximately 5-10 minutes.

**TOP REASONS TO STAY AT RENAISSANCE PALM SPRING HOTEL**

- No Commute! All conference events are taking place at the Convention Center – attached to the Hotel
- Only 10 Minutes from the Palm Springs Airport
- Complimentary wireless internet in your guest room
- Downtown Palm Springs restaurant and shops are just minutes from the hotel
- Nearby attractions such as The Palm Spring Aerial Tramway to experience the breathtaking journey up the Chino Canyon is just minutes away

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Generate more targeted, qualified leads within life sciences with CHI’s Lead Generation programs. We will mine our database of 800,000+ life science professionals to your specific needs. We guarantee a minimum of 100 leads per program! Opportunities include:

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- Podcasts

Advertising opportunities such as marketing and promotional emails are also available.

**To customize your participation at this event, please contact:**

- **Companies A - K:**  
  Jason Gerardi  
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  jgerardi@healthtech.com

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**SPONSORSHIP, EXHIBIT, AND LEAD GENERATION OPPORTUNITIES**

CHI offers comprehensive sponsorship packages which include presentation opportunities, exhibit space and branding, as well as the use of the pre- and post-show delegate lists. Customizable sponsorship packages allow you to achieve your objectives before, during, and long after the event. Signing on early will allow you to maximize exposure to qualified decision-makers!

**AGENDA, BREAKFAST, AND LUNCHEON PRESENTATIONS**

Showcase your solutions to a guaranteed, highly-targeted audience. Package includes a 15 or 30-minute podium presentation within the scientific agenda, exhibit space, on-site branding, and access to cooperative marketing efforts by CHI. For the luncheon option, boxed lunches are delivered into the main session room. Presentations will sell out quickly. Sign on early to secure your talk!

**INVITATION-ONLY VIP DINNER/HOSPITALITY SUITE**

Sponsors will select their top prospects from the conference pre-registration list for an evening of networking at the hotel or at a choice local venue. CHI will extend invitations and deliver prospects.

*Inquire about additional branding opportunities!*
The course will begin with an overview of biophysical and biochemical properties of proteins. A typical development workflow (including statistical analysis and DOE elements) will be outlined to demonstrate the core elements employed during protein formulation. The course concludes with real-world examples from formulation development projects for both liquid and lyophilized products.

**Course Information:** Course is 1.5 days, and lunch is provided on the first full day. Course attendees will each receive a handbook with instructor presentation materials.
## Conference At-a-Glance

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### At-a-Glance

**Sunday (Jan. 12), 5:00-8:00 pm**
- Dinner Short Courses*

**Monday-Tuesday (Jan. 13-14)**
- Antibody Optimization and Development
- Enhancing Antibody Binding and Specificity

**Tuesday (Jan. 14), 5:00-8:00 pm**
- Improving the Clinical Efficacy of Antibody Therapeutics
- Turning Antibodies into Drug Products

**Wednesday-Thursday (Jan. 15-16)**
- Antibody-Drug Conjugates
- Bispecific Antibody Therapeutics

**Thursday-Friday (Jan. 16-17)**
- Protein Aggregation: Mechanism and Characterization
- Lyophilization and Emerging Drying Technologies

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**PepTalk BuzZ Sessions**

BuzZ Sessions are facilitated, small-group discussions. Interactive participation leads to problem-solving solutions and future collaborations around focused topics.

If you have a topic idea or would like to moderate a table, please contact: Ann Nguyen at anguyen@healthtech.com

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**Get Connected!**

**CHI’s INTRONET**

Networking at its Best

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 that 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.

**PepTalk Event App**

New this year, the PepTalk App will allow attendees to browse the agenda, create custom schedules, navigate the exhibit hall and explore poster presentations. Visit chi-peptalk.com for more information and availability.
We have developed a powerful recombinant-based strategy for generating customized synthetic antibodies by integrating a set of wholly in vitro techniques into an automated high-throughput pipeline. The task involved designing novel phage display libraries, improved biopanning techniques, optimizing small-scale screening and purification techniques all networked together by modern lab automation systems. Developed recombinant antibody generation process requires efficient production of highly purified proteins and streamlined quality control which will be discussed in detail.
2:35 Bacterial Chromosomal Engineering for Optimization of Protein Expression and Function

Joseph Kittle, Jr., Ph.D., Assistant Professor, Chemistry and Biochemistry, Ohio University and CSO, Molecular Technologies Laboratories, LLC

We have used chromosomal engineering to develop advanced bacterial strains and methods for improved expression of therapeutic and research proteins. Modified expression of bacterial host genes alters bacterial metabolism and improves fermentation. Rapid chromosomal engineering methods for generating gene variants facilitate some protein variants with improved function and/or stability. We will document the performance of engineered strains and proteins compared to traditional plasmid-based systems and show how gene variant screening can help solve problems in antibody fragment-based protein expression.

3:05 Molecular Evolution of Human Butyrylcholinesterase

John Cashman, Ph.D., President and Founder, Human BioMolecular Research Institute

From random cDNA libraries, using a medium throughput screen, molecular evolution of human butyrylcholinesterase was accomplished. Several promising organophosphate detoxication catalysts were identified.

3:35 New Endotoxin-Free E. coli Cell Strains for Plasmid and Protein Production without Endotoxin Removal

Curtis Knox, Vice President, Marketing & Sales, Lucigen Corp.

Lucigen will present novel competent E. coli cell strains lacking lipopolysaccharide (LPS) for endotoxin-free protein and DNA production. Examples of endotoxin reduction levels achieved with Lymulus Amoebocyte Lysate (LAL) and human cell line-based assays will be demonstrated, as well as protein expression and plasmid production experimental data.

3:50 Refreshment Break

4:15 Screening Antibody Phage Libraries in Product Format

Partha Chowdhury, Ph.D., Principal Scientist, Antibody Discovery and Protein Engineering, MedImmune, Inc.

Despite being a powerful technology for antibody discovery, phage libraries are severely limited because they cannot be directly screened in a relevant product format which is typically IgG. This talk will focus on the development and validation of a new technology that enables batch conversion of scFvs from phage libraries and high-throughput screening as IgGs.

FEATUR ED PRESENTATION

4:45 Genetic Engineering and Preclinical Testing of Salmonella Live Vaccines

James E. Galen, Ph.D., Professor, Medicine, Chief, Salmonella Live Vector Vaccine Section, University of Maryland School of Medicine

The genetic engineering of attenuated Salmonella Typhi live vector vaccines, capable of delivering protective antigens from unrelated human pathogens, will be described, with emphasis on the development of live vaccines against plague. The immunogenicity and protective efficacy in mice of our novel vaccines will be also be presented.

5:30 Close of Session

5:45-7:00 Welcome Reception in the Exhibit Hall with Poster Viewing

FEATURED PRESENTATION

8:35 Molecular Cloning, Overexpression and an Efficient One-Step Purification of αVβ5 and α5β1 Integrin

Lawrence J. Tartaglia, Ph.D., Research Scientist, Biochemistry and Molecular Biology, Center for Structural Biology, University of Florida Recombinant αVβ5 and α5β1 integrin expression systems were created for the large-scale production of integrin extracellular domains that take advantage of Fos and Jun dimerization for expression in HEK293 cells and SF9 insect cells. Both integrin heterodimers were purified in a one-step nickel column purification scheme, characterized and yields were in quantities suitable for multiple applications including structural biology and functional assays.

9:05 Brevibacillus, a New Tool for High-Level Intracellular Expression of Bacterial Antigens

Domenico Maione, Ph.D., Unit Head, Cloning and Expression, Novartis Vaccines and Diagnostics

Brevibacillus coagulans, a novel Gram positive Expression System, is an easy-to-handle non-sporulating bacterium. One major drawback that limits applicability is the absence of expression vectors based on inducible promoters. We achieved high level of intracellular protein expression in Brevibacillus, using the phis1522 vector carrying the B. megaterium xylose-inducible promoter (PxyLA). Our results suggest that the intracellular protein expression in Brevibacillus could be an attractive strategy to produce proteins that are poorly expressed, toxic or degraded in E. coli.


Armagan Ozgür, Research Scientist, Institute of Molecular Enzyme Technology, Forschungszentrum Jülich, Heinrich-Heine University

The intricate nature of membrane proteins hampers their structural and functional studies because common expression hosts like E. coli are optimized for the production of soluble proteins. Therefore, we developed a new expression system based on the facultative phototrophic non-sulfur purple bacterium Rhodobacter capsulatus. Protein accumulation and localization studies revealed that E. coli seems to be the preferable expression host for human membrane proteins with low number of transmembrane helices, whereas membrane proteins with a higher number of transmembrane domains achieve higher protein yields with the newly developed R. capsulatus expression system. Therefore, the photosynthetic bacterium R. capsulatus is a promising alternative platform organism for the heterologous expression of more complex membrane proteins.
Pipeline 5: EXPRESSION AND PRODUCTION

Sixth Annual
January 13-14

Engineering Genes, Vectors, Constructs and Clones
Upstream Decisions Lead to Downstream Success

9:50 Coffee Break in the Exhibit Hall with Poster Viewing

10:50 A New and Versatile Concept for Systematic Multi-Gene Constructs Generation
Wassim Abdulrahman, Ph.D., Research Scientist, Mechanisms of Cancer, Friedrich Miescher Institute for Biomedical Research and CPC Novartis

Protein complexes expression is a major challenge for drug discovery. Although several molecular biology methods are well established for generating multi-gene constructs, none of these methods are adapted to in-parallel screening strategies. I will describe a novel and versatile method specifically designed for robotized screening of multi-protein expression.

11:20 Data Management and Automation of Protein Production Workflows in Biologics R&D
Christoph Freiberg, Ph.D., Senior Scientist, Biologics Research, Bayer HealthCare

Our comprehensive workflow platform supports highly parallelized antibody and tool protein production. It uniquely integrates in silico cloning, construct annotation and molecule registration functionalities, while supporting automated and high-throughput evaluation of expression systems of different scales. The molecule's historical record is faithfully recorded, from early discovery campaigns to engineering and late-stage development. A single system stores molecule hierarchies and associated key expression, purification and analytics data. We thus glean essential information for improving product quality and optimizing production processes.

11:50 Sponsored Presentation (Opportunity Available)

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

2:00 Buzz Session A (Please visit our website for topics)

3:00 Refreshment Break in the Exhibit Hall with Poster Awards

3:45 Buzz Session B (Please visit our website for topics)

4:45 Close of Conference

4:30-5:00 Short Course Registration

5:00-8:00 Dinner Short Courses (SC8-SC14)
See page 3 for details

Present a Poster
Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions.

Reasons you should present your research poster at this conference:

• Your poster will be exposed to our international delegation
• Receive $50 off your registration
• Your poster abstract will be published in our conference materials
• You will automatically be entered into the poster competition
• Your research will be seen by leaders from top pharmaceutical, biotech, academic and government institutes

To secure a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by November 22, 2013.
Pipeline 5: EXPRESSION AND PRODUCTION

Sixteenth Annual
Recombinant Protein Expression and Production
Achieving Quality and Quantity

TUESDAY, JANUARY 14 (SEE PAGE 15 FOR DETAILS)

1:30-2:00 pm Conference Registration

WEDNESDAY, JANUARY 15

7:30 am Conference Registration
8:00 Morning Coffee

EXPRESSION: IMPROVING YIELDS

8:15 Chairperson’s Opening Remarks
Karl E. Griswold, Ph.D., Associate Professor, Thayer School of Engineering, Dartmouth College

» KEYNOTE PRESENTATION

8:20 Protein Expression Technologies: Evolution or Revolution? Lorenz M. Mayr, Ph.D., Vice President, Reagents & Assay Development, AstraZeneca, Inc.
Protein expression has long been viewed as a mature discipline, but current trends in drug discovery show an increased demand for fast, efficient expression systems. We will discuss comprehensive and contemporary activities in place for protein expression at AstraZeneca. Topics include an overview of established protein expression technologies; novel technologies and trends for protein expression in drug discovery research; case studies for difficult-to-express proteins and protein complexes; finding the balance between in-house efforts and outsourcing; and a summary and outlook.

9:00 Novel Strategy for Production of Difficult-to-Express Proteins in E. coli Based on an Anchored Periplasmic Expression System
Ki Jun Jeong, Ph.D., Assistant Professor, Chemical and Biomolecular Engineering, KAIST
For the efficient production of difficult-to-express proteins such as aggregation-prone proteins and lytic enzymes in the E. coli host, we have developed a new production system based on an Anchored Periplasmic Expression (APEX) system. In this APEX, protein aggregation and lytic activity can be prevented through anchoring of individual proteins to the inner membrane. This concept was successfully demonstrated with two model proteins (aggregation-prone human leptin and lytic lase).

9:30 Production of Disulfide-Rich Peptides via Expression in the Periplasm of Escherichia coli
Glenn F. King, Ph.D., Research Scientist, Institute for Molecular Bioscience, University of Queensland
Disulfide-rich venom peptides (DRPs) have received attention as potential therapeutics. However, expression of functional DRPs in the reducing environment of the E. coli cytoplasm is difficult. Thus, we developed a protocol for DRP expression in the E. coli periplasm, which houses the machinery for disulfide-bond formation. We demonstrate this method for production of a wide range of DRPs (2–8 kDa, 2–6 disulfide bonds).

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

10:45 A Simple PiggyBac Transposon-Based Mammalian Cell Expression System for Inducible Protein Production
James M. Rini, Ph.D., Professor, Molecular Genetics and Biochemistry, University of Toronto
We have developed a doxycycline inducible PiggyBac (PB) transposase-based mammalian cell expression system which greatly simplifies the generation of stably transfected bulk cell cultures for protein production. It works with both adherent and suspension-adapted cell lines and owing to the efficiency of PB-mediated integration, the system allows for the generation of bulk cell cultures in 96-well format. Our interests are focused on secreted and membrane proteins and the utility of the system will be demonstrated with a number of examples.

11:15 High-Throughput Imaging to Increase the Assurance of Clonality during Cell Line Development
David Shaw, Ph.D., Scientist, Early Stage Cell Culture, Genentech, Inc.
Current methodologies to create monoclonal cell lines include limiting dilution or single-cell sorting at conditions that offer statistical assurance of monoclonality. We are evaluating a fluorescent high-throughput automated imaging workflow that can provide direct evidence on whether the cell line originated from one cell during the cloning step. We will discuss some of the challenges during the development of this protocol and provide case study data.

11:45 Cell Line Development: Can Modifications at the Early Stages Improve Therapeutic Cell Line Selection?
Bernie Sweeney, Ph.D., Senior Group Leader, Mammalian Expression, UCB
The generation of manufacturing cell lines can require screening 100s-1000s of clones. High-throughput technologies have enabled more efficient screening but modifications in early stages of cell line manufacturing may help further. Approaches include the use of engineered cell lines, chromatin modifying elements and overexpression of “helper” proteins. We will present data on some approaches and demonstrate how they can shorten timelines and reduce costs during cell line development.

12:15 pm Selexis SURE CHO-Mplus™ Libraries: Custom Solutions for Protein Expression Bottlenecks
Igor Fisch, Ph.D., CEO, Selexis SA
Ideal protein expression systems should both boost transcription as well as address expression bottlenecks. For the newest SUREtechnology innovation, Selexis leveraged data from the completed SURE CHO-M Genome and Transcriptome project to engineer the SURE CHO-Mplus Libraries designed to address expression issues in CHO-M cells. Selexis’ expression technology doesn’t need antibiotic selection, allowing for screening of multiple auxillary proteins simultaneously. These libraries boost expression over a broad range of difficult-to-express proteins.

12:45 Luncheon Presentation: Why Are You Still Doing Westerns?
John Proctor, Ph.D., Director, Corporate Development, ProteinSimple
If you are, you must not know about the Simple Western, a gel-free, blot-free, hands-free reinvention of the traditional Western blot. It is a fully automated family of instruments that delivers reproducibility and true quantitation while drastically reducing the hands-on time required when performing a traditional Western. In this presentation, I will illustrate examples of how the Simple Western has been applied in protein expression and production, cell signaling analysis, biotherapeutic characterization and vaccine research.

PURIFICATION: IMPROVING PRODUCT QUALITY

1:15 Chairperson’s Remarks
James M. Rini, Ph.D., Professor, Molecular Genetics and Biochemistry, University of Toronto

1:55 Microbial Production of Folded and Fully Functional Antibacterial Enzymes
Karl E. Griswold, Ph.D., Associate Professor, Thayer School of Engineering, Dartmouth College
Widespread drug resistance among bacterial pathogens has focused increasing attention on antibacterial biocatalysts and their clinical application. In particular, genetically engineered versions of natural enzymes have the potential to exert powerful therapeutic effects, but scalable production systems, able to service early-stage discovery and development through pilot or production-scale translation, are often lacking. This talk will highlight recent advances in expression and purification from Escherichia coli and Pichia pastoris.

2:20 A Yeast-Based Platform for High-Yield, High-Quality Production and Purification of Eukaryotic Membrane Proteins
Per Amstrup Pedersen, Ph.D., Professor, Biology, University of Copenhagen
Membrane proteins are by far the single group of proteins most difficult...
to express and purify in a functional form. Engineering expression and solubilization conditions have allowed us to produce high-quality eukaryotic membrane proteins in quantities allowing fundamental protein chemical analysis as well as exploiting their use in industrial applications.

2:45 Optimizing Expression Tags and Fermentation for Production of Functional Human Integral Membrane Protein Receptor
Alexei Yeliseev, Ph.D., Staff Scientist, Protein Biochemistry, LMBB, National Institutes of Health
Human cannabinoid receptor CB2 is an important target for pharmaceutical drug development. We optimized production of the functional CB2 receptor, labeling with stable isotopes by fermentation in E. coli, and efficient purification of the receptor by testing expression hosts, cultivation conditions and different combination of affinity tags including C-terminal nanoparticle (Rho-tag). The purified, stable receptor reconstituted into liposomes is amenable to studies by solid-state nuclear magnetic resonance spectroscopy.

3:10 Reversible Labeling of Native and Fusion-Proteins
Michael D. Burkart, Ph.D., Professor, Chemistry and Biochemistry, University of California, San Diego
The reversible covalent attachment of chemical probes to proteins has long been sought as a means to visualize and manipulate proteins. We have developed the full reversibility of post-translational custom panethelene modification of carrier protein domains and fusion protein for visualization and functional studies. This iterative enzymatic methodology can be used in vitro to reversibly label protein variants for a variety of applications, including isolation, visualization and immobilization.

3:35 Discovery Protein Expression Enabled by Pfénex Expression Technology™
Russell Coleman, Senior Scientist, Pfénex Inc.
Discovery scientists’ first step in every product development program is the acquisition of active protein. Leveraging the high-throughput Pfénex Expression Technology™ platform, milligram amounts of purified proteins can be produced in support of early stage in vitro and in vivo evaluation. Case studies will provide an overview regarding how Pfénex scientists accomplish this task.

3:50 Refreshment Break

4:15 Unfolded Protein Response (UPR) During CHO Cell Production Product Quality
Zhimei Du, Ph.D., Senior Scientist, Cell Sciences & Technology, Amgen, Inc.
We have created a UPR-responsive, fluorescence-based reporter system to detect and quantify specific UPR-mediated transcriptional activation of intracellular signaling pathways in real time without manipulation. The results showed the UPR activation is dynamically regulated during production culture. Also, the clones differed in their UPR induction patterns; the timing and the degree of UPR-induced transcriptional activation were linked to the growth, viability, productivity and product quality of the cells.

4:45 Engineering a Mammalian Cell Line Toolkit that Exhibits Multiple Productivity and Product Quality Profiles
Mark Tié, Associate Scientist, Cell Culture Development, Biogen Idec
We have engineered new mammalian host cell lines that broaden the range of achievable product quality attributes. This lets us match a molecule of interest to one of our new host cell lines at the onset of cell line development. We will show data of our in-depth characterizations of these host cell lines using model receptor-FC fusion and monoclonal antibody molecules. Our results demonstrate that different host cell lines can occupy distinct areas of product quality and productivity space.

5:15-6:30 Reception in the Exhibit Hall with Poster Viewing

THURSDAY, JANUARY 16

7:15 am Conference Registration
7:30 Breakfast Presentation (Sponsorship Opportunity Available) or Morning Coffee
PipeLine 5: EXPRESSION AND PRODUCTION
Inaugural
Transient Protein Production
From Small-Scale to Large-Scale

THURSDAY, JANUARY 16
1:00-1:45 pm Conference Registration

CELL LINES: NEW DEVELOPMENTS

2:00 Chairperson’s Opening Remarks
Athena Wong, Ph.D., Scientist, Early Stage Cell Culture, Genentech, Inc.

KEYNOTE PRESENTATION

2:05 Recombinant Protein Production in Transient Fashion: A Mature Technology?
Sabine Geisse, Ph.D., Director/NLS, Novartis Institutes for BioMedical Research
The huge wealth of recombinant proteins generated by transient expression, as well as the availability of well-documented protocols in the public domain, reflects the remarkable success of transient protein production over the past 15 years. Thus, the term “mature technology” seems justified – yet, process gaps and shortcomings do exist. The presentation will cover a brief overview on our currently applied routes to protein production (including the novel CAP-T™ expression system) and address some of the issues encountered and future perspectives.

2:45 Application of a New Human Cell Line, F2N78, as a Host Cell for Transient Production of Biopharmaceuticals
Jong-Mook Kim, Ph.D., Director, Cell Science Team, R&D Division, Celltrion Inc.
F2N78, generated by a somatic fusion of 293 cells with Namalwa cells, showed a constitutive expression of EBNA1, and human-specific glycosylation enzymes, GnTIII and α2,6ST, for over one year under serum-free suspension culture conditions. Monoclonal antibody (mAb) productivity of ~100 μg/ml was obtainable six days post-transfection with oriP expression vector and the produced mAb could be applied for a selection of proper mAb during early development process of a new target molecule.

3:15 Use of an Anti-Apoptotic Cell Line for High-Throughput Transient Gene Expression
Athena Wong, Ph.D., Scientist, Early Stage Cell Culture, Genentech, Inc.
This presentation describes the development of a polyethylenimine (PEI) transient transfection system using an anti-apoptotic CHO-K1 host cell line generated by deleting two pro-apoptotic factors, Bax and Bak, using zinc finger nuclease-mediated gene disruption. The Bax Bak double knockout (DKO) cells expressed 3-4 fold higher antibody titers than CHO-K1 cells, maintained higher viability post-transfection and had decreased active caspase-3. The optimized high-throughput process can be used for scales ranging from automated tube spins and shake flasks to stirred tank bioreactors.

3:45 The Impact of Scalable Transient Gene Expression: Maximizing CHO Antibody Production to Accelerate Project Timelines
James Brady, Ph.D., Director, Technical Applications, MaxCyte, Inc.
CHO transient gene expression (TGE) greatly accelerates antibody development by eliminating the need to change cell backgrounds during scale up to biomanufacturing. Data using MaxCyte transient transfection will be presented demonstrating its scalability, the production of antibody titers >1g/L, and the rapid generation of high yield stable CHO cell lines.

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

4:45 Rapid Screening of Membrane Protein Expression in Transiently Transfected Insect Cells
Hao Chen, Ph.D., Senior Scientist, Protein Technologies, Amgen, Inc.
Membrane proteins play critical roles in many biological processes and are the focus of intense biomedical research. One bottleneck for studying membrane proteins is the difficulty in expressing correctly folded and stable proteins, which often requires time and resource-intensive protein engineering and optimization. Here, we present an ultrasensitive method for rapidly screening membrane protein expression in insect cells, in which only nanogram levels of unpurified proteins are required.

5:15 Optimized Signal Peptides for the Development of High-Expressing CHO Cell Lines
Lars Kobert, Ph.D., Scientist, Cellica GmbH
Powerful signal peptides: Mammalian cell lines are the first choice for the production of biotherapeutic secretory proteins. In our last article we identified two very potent human-derived signal peptides suitable for the production of biopharmaceutical proteins. With these signal peptides we were able to generate highly productive mammalian cell lines with cell-specific productivities up to 90 g/pcell and day. Furthermore, we have obtained product concentrations up to 4 g per liter in a protein-free chemical defined cell culture medium.

5:45 Close of Day

FRIDAY, JANUARY 17
7:15 am Conference Registration

7:30 Breakfast Presentation (Sponsorship Opportunity Available) or Morning Coffee

CELL LINES: PLANTS

8:30 Chairperson’s Remarks
Peter Gray, Ph.D., Director, Australian Institute for Bioengineering and Nanotechnology, University of Queensland

8:35 Transient Plant Production of Therapeutic Molecules to Prevent Viral Transmission and Neurotoxicity in Macaques
Yvonne J. Rosenberg, Ph.D., CEO, PlantVax, Inc.
(I) Agrobacterium-mediated transient transfection of two Nicotiana species has been tested to rapidly produce high levels of both HIV envelope and several broadly neutralizing anti-HIV monoclonal antibodies to evaluate their HIV inhibitory properties, to assess their pharmacokinetics and their ability to passively prevent transmission of HIV. (II) A bioscavenger pretreatment is being developed to prevent neurotoxicity following exposure to organophosphate pesticides and nerve agents.

9:05 Plant-Produced Human Recombinant Erythropoietic Growth Factors Support Erythropoietin Differentiation in vitro
R. Mark Jones, Ph.D., Senior Scientist, Fraunhofer USA Center for Molecular Biotechnology
Human growth factors erythropoietin (EPO), stem cell factor (SCF), interleukin 3 (IL3) and insulin-like growth factor-1 (IGF-1) were expressed in plants using a Tobacco mosaic virus vector-based transient expression system. By comparing EC50 values of plant-produced cytokines with standards, we have demonstrated that all four plant-produced growth factors stimulated the expansion of umbilical cord blood-derived CD34+ cells and their differentiation towards erythropoietic precursors with the same potency as commercially available growth factors.

9:35 Protein Body-Inducing Fusions for High-Level Accumulation and Purification of Recombinant Proteins in Plants
Rima Menassa, Ph.D., Research Scientist and Adjunct Professor, Biology, Agriculture and Agri-Food Canada, Western University
We have developed two fusion polypeptides, elastin-like polypeptides (ELP) and hydrophobin I (HFB1) that improve accumulation of recombinant proteins in plants by 2 to 100 fold. These tags also have physico-chemical properties which aid in non-chromatographic purification of the protein. We have tested these fusion tags in transient expression by Agrobacterium infiltration in Nicotiana benthamiana leaves, and will discuss results obtained with several industrial and pharmaceutical proteins.

10:05 Selected Oral Poster Presentation: Large-Scale Automation of Plasmid DNA Purification for Transient Mammalian Expression
Mark Nagel, Senior Research Associate, Protein Chemistry, Genentech, Inc.
A large-scale automated multi-plasmid DNA purification process utilizing the
GE Akta Xpress with a unique flow path design and off the shelf reagents will be presented. DNA purity was assessed using RT-PCR of each serial plasmid DNA purification and mock purifications post system cleaning. This technology improves FTE efficiency, is easily scalable, utilizes less lab space and lowers the cost per mg of purified DNA.

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

CELL LINES: STABLE OR TRANSIENT OR BOTH?

11:15 Transient and Stable Expression of the Neurotensin Receptor NTS1: A Comparison of the Baculovirus-Insect Cell and the T-REx-293 Expression Systems

Joseph Shiloach, Ph.D., Head, Biotechnology Core Laboratory, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), NIH

Baculovirus-infected insect cells and tetracycline-inducible mammalian cell lines are routinely used for G protein-coupled receptor (GPCR) production for crystallography purposes. A suspension T-REx-293 cell line stably expressing neurotensin receptor 1 (NTS1) was compared with the transient baculovirus-insect cell system throughout the expression and the purification. The two systems were comparable on aspects of functional NTS1 expression levels and receptor binding affinity. But NTS1 surface display on T-REx-293 cells was 2.8 fold higher than that on insect cells.

11:45 Productivity and Quality of Recombinant Proteins Produced by Stable CHO Cell Clones can be Predicted by Transient Expression in HEK Cells

Rüdiger Neef, Ph.D., Principal Scientist, USP Development, Amgen, Inc.

To facilitate biopharmaceutical lead candidate selection, we describe an approach that allows prediction of productivity and quality of recombinant proteins by stable cell clones with the help of transient transfection studies. This is exemplified for bispecific T cell engager (BiTE®)—a new class of single-chain antibody-based therapeutics. BiTE® titers and the percentage of monomeric BiTE® fractions in cell culture supernatant of transiently transfected HEK cells showed a striking correlation with titers and monomer yield of selected stable CHO cell clones.

12:15 pm Expression of Monoclonal Antibody Variants in Transient and Stable Cultures, the Effects of Sequence on Stability and Expression Level

Susan Sharfstein, Ph.D., Associate Professor, Nanobioscience, Nanoscale Science and Engineering, University at Albany, State University of New York

Antibody variants with different amino acids in Kabat position 49 were expressed in CHO cells using stable and transient transfection. Significant differences in expression were observed between two primary variants, Ala and Gly. In transient transfections, no correlation was seen between mRNA levels and protein expression; however, in stable clones a strong correlation was seen. These results show the critical relationship between sequence and productivity and increase the need for a deeper understanding of structure/function relationships in antibody engineering.

12:45 Combine Expression-Optimized Genes with High-Density 293 Cultures to Maximize Protein Yields

Sponsored by Life Technologies

Henry C. Chiu, Ph.D., Senior Product Manager, Life Technologies

Life Technologies has developed cutting-edge gene optimization and gene synthesis technologies that can be coupled with the ExpI293 high-density expression system to achieve gram-per-liter protein yields. Users can apply these technologies in their laboratories to generate the highest expression levels possible, or outsource the entire process to obtain their desired proteins within six weeks.

2:00 Chairperson’s Remarks

Richard Altman, MS, Research Scientist, Alexion Pharmaceuticals

2:05 Production of Human Full-Length PPARγ2 in HEK293 Cells by Transient Expression

Jianming Liu, Ph.D., Senior Scientist, Discovery Sciences, AstraZeneca, Inc.

Recombinant human full-length peroxisome proliferator-activated receptor gamma 2 (PPARγ2) was successfully expressed in HEK293-6E cells by transient expression; the expression level is > 10 mg per liter culture. An efficient purification method was developed to obtain full-length PPARγ with high purity. Functional properties of the recombinant PPARγ were also demonstrated.

2:35 High-Throughput Mammalian Expression of Antibodies Enabling Functional Screening in Product Format

Robin Butler, Senior R&D Manager, Protein Sciences, Antibody Discovery and Protein Engineering, MedImmune

This presentation will provide an overview of the current process which produces large numbers of research-scale IgG supporting antibody discovery at MedImmune. I will introduce a new platform process developed at MedImmune using a novel cloning procedure and automated transient expression in mammalian cells, capable of delivering thousands of IgG proteins per week suitable for in vitro biochemical and cell-based high-throughput screening.

3:05 Optimising Transient Gene Expression

Katharine Cain, Ph.D., Principal Scientist, Protein Expression and Purification Group, UCB

A transient expression system has been developed at UCB. This system employs a number of culture conditions which have provided incremental increases to transient antibody yields. The most substantial impact on yield was observed when using a CHO host that was engineered to express exogenous XB1-S and ERO1La. The generation of this CHO host (CHO-SXE) will be described and how this cell line and transient culture conditions have improved our antibody yields.

FEATURED PRESENTATION
3:35 Epi-CHO, a Novel CHO Cell Line Capable of High-Level Transient Protein Productivity

Peter Gray, Ph.D., Director, Australian Institute for Bioengineering and Nanotechnology, University of Queensland

The Epi-CHO cell lines have been engineered to promote the replication and maintenance of episomal plasmid DNA during cell growth. This allows the cell numbers to be expanded following transfection, and the culture volume...
SUNDAY, JANUARY 12

4:00-5:00 pm Short Course Registration
5:00-8:00 Dinner Short Courses (SC1-SC7)
See page 3 for details

4:00-8:00 Main Conference Registration

MONDAY, JANUARY 13

7:30 am Conference Registration and Morning Coffee

PROCESS DEVELOPMENT TOWARDS IMPROVEMENT

9:00 Chairperson’s Opening Remarks
Jennifer Nemeth, Ph.D., Associate Scientific Director and Head, Biologics Mass Spectrometry & Allied Technologies, Janssen R&D LLC

KEYNOTE PRESENTATION
9:10 From Protein Purification to Vaccine Development – A Challenging but Rewarding Journey
Yan-ping Yang, Ph.D., Director, Downstream Processing, Bioprocess Research & Development, Sanofi Pasteur
The vaccine industry is fraught with high risk, long cycle times and requires approximately 12 years to bring a product from preclinical to licensure at a cost of $1 billion. Purification of protein antigens to achieve consistent product purity and quality is an integral part of the protein-based product development process. This presentation focuses on the challenges encountered by protein purification scientists and the rewarding experiences in the journey of vaccine development.

9:50 Insight in the Formation of DNA-Protein Precipitates During Downstream Processing and Implications for Process Development
André Dumetz, Ph.D., Investigator, GlaxoSmithKline
Precipitation during downstream processing is a common problem that can undermine the scalability of a process. DNA-protein precipitates and coacervates, due to the carryover of small amount of DNA, often form in capture step eluates or during chromatographic cleaning steps. Several cases of study are presented and compared to the behavior observed on a DNA-protein model system to identify the main experimental trends. The implications for downstream process development and process robustness are discussed.

10:20 Coffee Break

10:45 Purification Strategies and Considerations in Overproduction, Isolation and Reconstitution of Labile Metalloproteins
Gareth Butland, Ph.D., Staff Scientist, Lawrence Berkeley National Laboratory
Iron-sulfur (FeS) cluster cofactors are ancient cofactors, built for an anaerobic environment, yet are present in all kingdoms of life and essential for viability. FeS clusters can be damaged by molecular oxygen and reactive oxygen species depending on redox potential and solvent accessibility. The isolation of FeS cluster containing proteins in a biologically relevant and homogeneous form can therefore be challenging. I will present some of the strategies we utilize to produce and isolate FeS proteins in a bioactive form.

11:15 Bacterial Strains Based on the Separatome of Escherichia coli
Ellen Brune, Ph.D., CSO, Boston Mountain Biotech
Improvement in throughput for recombinant biologic products can be realized by decreasing the amount of host cell proteins that interact with separation media as either binding proteins that reduce column capacity or eluting proteins that complicate gradient design. In an effort to streamline bioprocessing, our group has begun to rewrite the E. coli genome to substantially reduce the burden on purification steps, focusing on two popular bioseparation methods (Immobilized Metal Affinity Chromatography and Ion Exchange Chromatography).

11:45 Endotoxin Removal from Proteins Expressed in E. coli
Barry Holwerda, Ph.D., President, Molecular Throughput, Inc.
Preclinical evaluation of recombinant protein therapeutics requires the purification of proteins containing very low levels of endotoxin. Proteins expressed in E. coli present a special challenge because of their source and often require methods that are specific to each protein. This talk will summarize general principles and approaches to removing endotoxin highlighted by specific examples.

12:15 pm Addressing Purification Challenges for Recombinant Proteins Expressed in Non-Mammalian Systems
Shannon Ryan, Ph.D., Process Development Scientist, EMD Millipore Corporation
The templated nature of MAb purification processes has simplified PD activities significantly. However, many new biotherapeutics continued to be developed in microbial expression systems. Process Development for these products can be an issue due to both challenging aspects of microbial expression and the fact that a template for purification does not exist. This talk will discuss key aspects of purification Process Development with for recombinant proteins expressed in microbial systems.

12:45 Luncheon Presentation (Sponsorship Opportunity Available) or Lunch on Your Own
CONTINUOUS PROCESSING AND TECHNOLOGIES THAT SUPPORT PROTEIN PURIFICATION

2:00 Chairperson’s Remarks
Ellen Brune, Ph.D., CSO, Boston Mountain Biotech

2:05 Downstream Processing of Biologics Using Twin-Countercurrent Chromatography
Thomas Müller-Späth, Ph.D., CSO, ChromaCon AG
A novel twin-column, countercurrent sequential capture process (CaptureSMB) has been developed combining high-throughput with high capacity and allowing the optimal utilization of the stationary phase at reduced buffer consumption. For polishing steps, another twin-column chromatography process (MCSP) is being used with the same twin column equipment. In this presentation, case studies for the purification of antibodies are presented using both processes. Column loading, productivity and buffer consumption will be discussed in comparison to single column batch chromatography.

2:35 IQGAP1 Protein Purification and X-Ray Crystallography
Vinodh Kurella, Ph.D., Research Fellow, Bioinformatics, Harvard Medical School
Protein purification process is a prelude to X-ray crystallography. A case study will be presented on IQGAP1, a scaffold protein overexpressed in colon cancer. IQGAP1 Calponin Homology domain was purified but precipitated before crystallization trials. Re-designing the construct lead to stabilization and also yielded high-quality crystals. However, in-house diffraction pattern revealed a fragile crystal. Finally, a synchrotron beam was utilized to solve the structure to 2.4 Å. Isothermal titration calorimetry was performed with substrate to reveal mode of interactions.

3:05 Mass Spectrometric Applications for Assessing and Characterizing Biologics for Driving Development Success
Jennifer Nemeth, Ph.D., Associate Scientific Director and Head, Biologics Mass Spectrometry & Allied Technologies, Janssen R&D LLC
There are a host of mass spectrometric applications that can be applied to the evaluation of a biologic for the purpose of assessing the therapeutics’ potential for success in development. These studies include purity evaluations, structure susceptibility assessments, stress assessments, and lot-to-lot comparability studies. This presentation will present an overview of useful assays / study designs, as well as case studies highlighting their use on therapeutics.

3:35 Versatile Use of Mixed-Mode Sorbents for Removal of Aggregates from Monoclonal Antibodies
Yamuna Dasarathy, Ph.D., Director, Marketing, Pall Life Sciences
Biopharmaceutical manufacturing requires high quality process development...
resulting in maximum degree of purity. Some biopharmaceuticals show a penchant for aggregating in solution the causes of which are still under investigation including high concentrations of target proteins as well as various stresses produced during downstream bioprocessing steps. Aggregation has been found to be a cause of immunogenicity and it reduces productivity of a process by impacting purity, recovery and yield. Additionally, host cell proteins that are inherent to all production processes can reduce efficacy. Mixed mode chromatography can be used to remove aggregates and other trace contaminants including host cell proteins and we will present a case study to elucidate the mixed mode mechanism.

3:50 Refreshment Break

**PURIFYING ANTIBODIES**

4:15 Development of a Non-Protein A MAb Capture Step Based on Selective Precipitation Combined with CEX
Guy de Roo, Ph.D., Project Leader, Downstream Processing, Biopharmaceuticals, Synthon

A process was developed which uses selective precipitation combined with a novel cationic (CEX) resin as the initial purification step. Several CEX resins were evaluated for binding capacity, selectivity and cleanliness. The selected CEX resin has a significant increased capacity over protein A and data indicate a purity which is nearly equal to a typical protein A eluate. The initial data show that the combined use of selective precipitation and CEX are promising for future “high” titer antibody purification processes.

4:45 Development of a Goat Polyclonal Antibody Purification Process for Improved Yield and Stability
Steven P. Allen, Ph.D., Manager, Biologics Process Design R&D, Diagnostics R&D, Abbott

A purification process for a goat polyclonal antibody has been redesigned to improve product quality and reduce production costs. A two-step purification process has been developed to improve low process yields due to high amounts of aggregate and precipitate. Mabsorbent is used in the initial capture step in separating out the polyclonal IgG population followed by an immunoaffinity column that separates out the target specific molecule with high purity (>90%), high specificity (≥100%), and improved final yield.

5:15 A Novel Cell Culture Flocculation Process to Streamline Antibody Purification and Downstream Processing
Kenneth (Yun) Kang, Ph.D., Principal Scientist, BioProcess Sciences, ImClone Systems, a wholly owned subsidiary of Eli Lilly & Co.

Recent advances in mammalian cell culture processes have significantly improved product titers, but have also resulted in substantial increases in cell density and cellular debris, and often increases in process and product-related impurities. In this study, we have developed a novel antibody harvest process that incorporates flocculation using a stimulus responsive polymer, benzylated poly(allylamine), followed by depth filtration. As tested on multiple antibodies, this process demonstrated high process yield, improved clearance of cells and cell debris, and efficient reduction of aggregates, host cell proteins (HCP) and DNA. This novel and efficient process can be easily integrated into current mAb purification platforms, and may mitigate downstream processing challenges.

5:45-7:00 Welcome Reception in the Exhibit Hall with Poster Viewing

**PURIFYING MEMBRANE PROTEINS**

10:50 Exploring Affinity Tags for Expression, Purification and Recovery of G Protein-Coupled Cannabinoid Receptor Type II (CB2)
Silvia Locatelli-Hoops, Ph.D., Scientist, Membrane Biochemistry and Biophysics, National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institutes of Health (NIH)

Human cannabinoid receptor type II (CB2), a G protein-coupled receptor (GPCR), regulates inflammation pathways. We explored the suitability of the affinity tags haloalkane dehalogenase (Halotag) and Rho-Tag (rhodopsin C-terminal nonapeptide) for expression of CB2 in E. coli and for efficient purification of functional receptor. The use of different strains, induction methods and constructs with alternating tag positions was explored. Methods for purification of the receptor by tandem affinity chromatography and surface immobilization were developed allowing further structural and functional studies.

11:20 New Chemical Tools for Stabilizing Membrane Proteins
Qinghai Zhang, Ph.D., Associate Professor, Integral Structural and Computational Biology, The Scripps Research Institute

We have designed beta-sheet peptides and steroid-based facial amphiphiles to stabilize integral membrane proteins. These novel amphiphiles are structurally distinct from classical detergents, and have enabled structural analysis of several membrane proteins by X-ray crystallography or electron microscopy. We will focus on the discussion of these chemical tools and respective applications in the structural dynamics studies of ATP-binding cassette transporters.
Higher-Throughput Protein Purification
Supporting Technologies

**TUESDAY, JANUARY 14**

1:30-2:00 pm Conference Registration

**BuzZ Sessions**

2:00 BuzZ Session A (Please visit our website for topics)
3:00 Refreshment Break in the Exhibit Hall with Poster Awards
3:45 BuzZ Session B (Please visit our website for topics)

4:30-5:00 Short Course Registration

5:00-8:00 Dinner Short Courses (SC8-SC14)

See page 3 for details

**WEDNESDAY, JANUARY 15**

7:30 am Conference Registration

8:00 Morning Coffee

**INDUSTRIAL SCALE HIGH-THROUGHPUT PROCESSING**

8:15 Chairperson's Opening Remarks
Ray Owens, Ph.D., NDM Senior Research Fellow, Division of Structural Biology, Oxford Protein Production Facility, University of Oxford

**KEYNOTE PRESENTATION**

8:20 High-Throughput Protein Expression & Drug Discovery – A Review
Ian Hunt, Ph.D., Group Leader, Protein Sciences, Novartis
A key ingredient to the successful identification and optimization of small-molecule compounds in drug discovery is the production of high quality recombinant proteins to help drive biochemical assays, biophysics and structural biology studies. This presentation will therefore review some of the key strategies developed to expedite protein production to support these needs and in a timescale’s commensurate with modern drug discovery processes. Topics covered will include the discussion of multi-parallel expression and purification strategies and the use of HT instrumentation for dealing with difficult to express proteins. The presentation will also use a series of case studies from a number of different projects to illustrate the impact of the various approaches in the support of drug discovery campaigns.

9:00 Directed Evolution of Enzymes on an Industrial Scale
Andrew Fosberry, Ph.D., Manager, Expression & Fermentation Sciences, Biological Reagents and Assay Development, PTS, GlaxoSmithKline Research & Development Limited
Processes for the production of pharmaceutical drugs and their precursors can potentially be made more efficient by the application of biocatalysts. This can have a beneficial effect on the reduction in cost of goods, reduction in the carbon footprint associated with the manufacture and vastly improve the sustainability of the process. Directed evolution can be utilised to alter an enzymes substrate profile and thus improve the function of that enzyme for a new substrate or reaction condition. We will give an industry insight into how we have developing our processes to tackle this challenge.

9:30 Case Study: Tools for High-Throughput DSP Development
Guy de Roo, Ph.D., Project Leader, Downstream Processing, Biopharmaceuticals, Synthon
A workflow was developed that proved effective in obtaining robust and scalable purification processes. The approach first assesses the molecule’s preferred environment before the actual purification development takes place. A case study will be presented in which a CEX step was developed for purification of an antibody using structural modeling, buffer screening, filter plates and Atoll columns followed by scale-up to 20 cm columns.

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

**HTP PROCESS DEVELOPMENT**

10:45 From Start to Finish, Applications of HTS to Accelerate Process Development
Ronald Gillespie, Ph.D., Scientist, Purification Process Development, Amgen, Inc.
Across the biotechnology industry, high-throughput screening (HTS) of chromatography resins for identifying optimal protein purification conditions has become an integral part of process development. In this talk, Amgen’s strategy for implementing high-throughput technologies for process development will be presented. Different HTS formats, such as micro-chromatography and batch binding in microfilter plate filters, will be compared for various applications such as candidate selection, process development and optimization. This talk will also emphasize Amgen’s efficiencies gained by data handling templates and close collaboration with our analytical teams to ensure decreased time from experimentation to data analysis.

11:15 Implementing a Buffer Optimization Screen into a High-Throughput Protein Production Core Service
William Gillette, Ph.D., Senior Scientist, SAIC-Frederick, Inc.
A core service protein production lab faces some unique problems in terms of buffer optimization. The huge diversity of targets and applications make it difficult to choose a one-size-fits-all approach. The talk will focus on the decisions we faced in choosing and implementing this platform with data from case studies presented to highlight the pros and cons of the approach.

11:45 A Multi-Platform Approach for High-Throughput Production of Secreted Proteins
Brandon Hillerich, Ph.D., Managing Director, High Throughput Protein Production, Albert Einstein College of Medicine
The Macromolecular Therapeutics Development Facility has developed and implemented a high-throughput pipeline for the production of secreted effector molecules. Through the use of robotics, the pipeline allows for rapid screening of protein expression in bacterial, insect and mammalian systems to determine what is best for scale-up production for structural and functional studies.

12:15 pm Application of Automated Purification Methods and Analysis for Process Development
Brian Gervie, Ph.D., Product Manager, PerkinElmer
LabChip® microfluidic technology enables the rapid analysis of multiple protein characterization including, molecular weight, purity assessment, N-glycans profiling, and charge heterogeneity. The JANUS® BioTx Pro Workstation provides researchers with the ability to run batch binding experiments in filter plate, tip-based chromatography, and miniaturized chromatography column formats on a single system. Together these approaches eliminate bottlenecks in sample preparation and characterization resulting in shorter development cycles and increased efficiency. We will present purification optimization case studies demonstrating 10X reduction in time and sample consumption relative to traditional approaches (e.g. FPLC). The detailed evaluation of scalability and application of these small-scale optimization studies illustrate the increased productivity for development and characterization of biotherapeutics as opposed to traditional methods.

12:45 Luncheon Presentation
(Sponsorship Opportunity Available) or Lunch On Your Own

**IMPROVING PROCESSES**

2:00 Chairperson’s Remarks
Brian Gervie, Ph.D., Product Manager, PerkinElmer

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will be discussed and illustrated by the results from recent projects. The extent to which lessons learned from the production of soluble proteins will be presented.

Efficient and reliable production of membrane proteins is critical for drug development for biologics. In this presentation the various formats routinely used for empirical assessment of separations performance will be reviewed, but the emphasis will be on the use of high-throughput methods for measuring fundamental chromatographic parameters and phenomena, such as adsorption isotherms and transport properties. The integration of such high-efficiency methods with established modeling approaches offers an alternative pathway for high-throughput chromatographic optimization.

Understanding the thermal stability and aggregation properties of proteins is important for a myriad of applications. Measurement of the thermal stability of a protein can be determined using either extrinsic or intrinsic fluorescence. This presentation will focus on a parallel measurement of protein thermal stability and aggregation. Case studies will be presented where this approach has been applied to optimize buffer selection and characterize protein-ligand interactions.

To facilitate high-throughput biochemical analyses of membrane proteins, we have developed a novel display technology in a microarray format. Both single-pass (CD4) and multiple-pass (GPR77) human transmembrane proteins were engineered to be displayed in the membrane envelope of herpes simplex virions. Purified virions and multiple-pass (GPR77) human transmembrane proteins were engineered to be displayed in the membrane envelope of herpes simplex virions. Purified virions printed on glass slides form a high-density Virion Display (VirD) Array. This method can be used to perform measurements of binding events involving large numbers of immobilised proteins in a time- and cost-effective manner. They are increasingly applied for high-throughput analyses, including antibody specificity screening, protein interactions and target discovery. A recent advance in technology is production of DNA-encoded protein microarrays through in situ cell-free synthesis directly from corresponding DNA arrays (DAPA method). This talk reviews recent developments in generation of protein microarrays and applications in proteomics and diagnostics.

At CHI-PepTalk.com, we believe in the power of high-throughput strategies to accelerate research and development. With the rapid pace of innovation in biopharmaceuticals, companies are moving towards high-throughput assays to meet analytical needs with accuracy, precision, and speed. Many technological improvements/breakthroughs in robotics and instrumentation have been made recently that have allowed for enhancements in the analysis of various critical attributes. This presentation will focus on the evolution of traditional methods to the most recent breakthroughs in high-throughput and advanced analytical technologies.

In this presentation, we will share recent developments in high-throughput and advanced analytical technologies used for screening and analysis of membrane proteins.
THURSDAY, JANUARY 16

1:00-1:45 pm Conference Registration

MECHANISM OF PROTEIN AGGREGATION

2:00 Chairperson’s Opening Remarks
Norman Garceau, Ph.D, CSO, Blue Sky BioServices, Inc.

KEYNOTE PRESENTATION

2:05 Mechanisms of Protein Aggregation
Thomas Laue, Ph.D, Professor, Biochemistry and Molecular Biology; Director, Biomolecular Interaction Technologies Center (BITC), University of New Hampshire

The forces that result in protein aggregation arise from various noncovalent interactions. Included in these interactions is the hydrophobic effect. This talk will focus on how the distance dependence of the hydrophobic effect may be incorporated in the proximity energy framework, and how various excipients modulate the hydrophobic effect.

2:45 The Effect of Formulation Factors on Opalescence in Protein Solutions
Ashlesha S. Raut, Ph.D. Candidate, Department of Pharmaceutical Sciences, University of Connecticut

The talk will discuss the theory of critical phenomena and the effect of formulation conditions on opalescence in protein solutions. The influence of protein-protein interactions on opalescence in the protein solutions will also be discussed.

3:15 Selected Oral Poster Presentation: Investigating Bioprocessing Variables That Influence Antibody Stability During Therapeutic IgG Production
Stephanie A. Davies, Postgraduate Research Student, Centre for Molecular Processing and School of Biosciences, University of Kent

The presence of particles and aggregates in biotherapeutic products is a concern for the manufacturers of such biologics due to the potentially associated immunogenic responses observed in some patients. In this work we have investigated the upstream and downstream bioprocess conditions that may induce or reduce IgG antibody particle formation. The two major findings from this work are firstly, varying culture stresses affects the levels of particles present in the final formulation; and secondly the inclusion of an additional wash step reduces the levels of these particles.

3:30 The Light Scattering Toolbox for Predicting and Characterizing Aggregation
Daniel Some, Ph.D, Principal Scientist, Wyatt Technology Corp.

Protein aggregates arise through a variety of pathways and take on many forms. Light scattering and related instrumentation constitute a powerful suite of tools that work in tandem to characterize absolute molar mass, size, charge and interactions of simple and conjugated proteins in solution, their propensity to aggregate and final aggregation states. This talk will review how essential light scattering techniques provided by Wyatt Technology inform the R&D processes for overcoming aggregation.

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

AGGREGATE CHARACTERIZATION AND PROTEIN STABILITY

4:45 Hydrogen-Deuterium Exchange Mass Spectrometry for Measurements of Protein-Protein Interactions
Jeffrey W. Hudgens, Ph.D., Research Chemist, Institute for Bioscience and Biotechnology Research, BioProcess Measurements Group, Biomolecular Measurement Division, NIST

Hydrogen-deuterium exchange mass spectrometry (HDX-MS) measures the exchange rates of amide hydrogens along protein chains. Since intra- and intermolecular hydrogen bonding within folded proteins can greatly slow amide hydrogen exchange, even small changes in protein tertiary structure can change the HDX profile. Thus, HDX-MS profiles report on the protein environment, including its folding configurations and binding interactions with adjacent proteins, as occurs in oligomers and aggregates.

5:15 Analytical Challenges in Detecting Protein Aggregates
Elizabeth M. Topp, Ph.D., Dane O. Kildsig Chair and Head, Department of Industrial and Physical Pharmacy, Purdue University

Aggregates are a common impurity in protein drug products, and can lead to potency changes and immunogenic response in patients. While various analytical methods can be used to detect aggregates, there is no single gold standard and different methods often give conflicting results. This presentation gives an overview of current methods for detecting and quantifying aggregates and suggests approaches for comprehensive product characterization.

5:45 Close of Day

FRIDAY, JANUARY 17

7:15 am Conference Registration

7:30 Breakfast Presentation (Sponsorship Opportunity Available) or Morning Coffee

PREDICTIVE TOOLS AND HIGH-THROUGHPUT SCREENING

8:30 Chairperson’s Remarks
Murali Bilikallahalli, Ph.D., Associate Director, Formulation Sciences, Proteins, Vaccines & Oligos, MedImmune

FEATURED PRESENTATION

8:35 Aggregation of Isolated Antibody Domains and Drug Conjugates
Dimiter S. Dimitrov, Ph.D., Senior Investigator, Protein Interaction Group, FNLCR, NCI, NIH

Aggregation of isolated antibody domains will be overviewed and our recent work on CH2 will be discussed in detail (Gong R et al Mol Pharm. 2013, unpublished). Aggregation of antibody drug conjugates (ADCs) will be also discussed. Experimental data and computational models will be presented for some of our ADCs.

9:05 Predictability and Implementation of HTS Technologies during Early Formulation Development
Hardeep Samra, Ph.D., Scientist II, Formulation Sciences Department, MedImmune, Inc.

9:35 High-Throughput Detection of Antibody Self-Interaction by Biolayer Interferometry
Yingda Xu, Ph.D., Group Leader, Protein Analytics, Adimab

Self-interaction of an antibody may lead to aggregation, low solubility or high viscosity. Rapid identification of highly developable leads remains challenging. Using bio-layer interferometry (BLI) technology, a high-throughput method to screen for antibodies prone to clone self-interaction (CSI) was developed that correlates well with SIC and CIC. This method allows hundreds of candidates to be screened in a matter of hours with minimal material consumption.

10:05 Selected Oral Poster Presentation: Peptide Aggregation Measurement and Prevention
Jeffrey Lampert, Research Scientist, Technical Service/Manufacturing Science, Eli Lilly and Company
Peptide aggregation can be controlled and even reversed by lowering pH without adjusting other parameters that have the potential to influence aggregation. A simple test using filtration and optical density measurements for quantifying aggregation was developed to allow time-point measurements and determination of aggregation rates.

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

**ANALYTICAL METHODS FOR ASSESSMENT OF PROTEIN AGGREGATION**

**11:15 Applications of Spin Labeling to Aggregated Proteins: A Sensitive Diagnostic Technique for Protein Structure, Folding and Misfolding**

Lawrence Berliner, Professor of Chemistry and Biochemistry, Chemistry and Biochemistry, University of Denver; Emeritus, Ohio State University

The spin labeling technique utilizes aminoxyl radical (nitroxide) labels which are tailored to either covalently or non-covalently bind to the system of choice. The distinct advantage of electron spin resonance electron paramagnetic resonance (EPR or ESR) is the sensitivity to protein motion with a unique marker of aggregation. It is not complicated by optical opacity and solids or aggregates.

**11:45 Detecting the Aggregation Propensity of Proteins by Bis-ANS: Binding Kinetics and Thermodynamics**

Murali Bilkallahali, Ph.D., Associate Director, Formulation Sciences, Proteins, Vaccines & Oligos, MedImmune

Aggregation is a major concern in therapeutic protein formulations especially in liquid form for extended shelf life. Aggregate levels often grow with time and detection of aggregation prone precursor is a challenging task in protein science. In this study we have used Bis-ANS, an hydrophobic ligand, to probe the aggregation propensity of different classes of IgGs and human serum albumin in native and physically stressed conditions. Calorimetric and millisecond fast kinetic studies are used to evaluate the thermodynamics and kinetics of ligand binding and evaluate the aggregation propensity of proteins.

**FEATURED PRESENTATION**

**12:15 pm Fluorogenic Tagging to Rapidly Screen for Oxidized and Covalently Aggregated Proteins**

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

To efficiently monitor protein oxidation and/or covalent aggregates, we developed and optimized a methodology for fluorogenic tagging, using either HPLC-fluorescence detection/mass spectrometry, SEC-fluorescence detection or fluorescence detection on a plate reader. This technique enables the detection of phenylalanine and tyrosine oxidation, products which are present in significant amounts in serum albumin in native and physically stressed conditions. Calibration and millisecond fast kinetic studies are used to evaluate the thermodynamics and kinetics of ligand binding and evaluate the aggregation propensity of proteins.

**12:45 Mid-Infrared Method for Protein Quantitation, Antibodies Aggregation Monitoring and Lipid Content Analysis of Biological Samples**

Ivona Strug, Ph.D., Senior Biochemical Scientist, EMD Millipore

Biological samples represent a range of complexities from homogeneous purified protein to multi-component mixtures containing proteins, aggregates, lipids and other macromolecules. The ability to accurately qualify these samples is paramount to downstream applications. Here we present a novel analytical method based on mid-infrared (MIR) spectroscopy that offers protein quantitation, possibility to monitor HCP and antibodies aggregation, analysis of lipid or detergent species, as well as the identification of other biomolecules, present in biological samples.

1:15 Luncheon Presentation: Counting and Sizing Protein Aggregates Down to 0.15 um in sub-mL Samples Using New Focused Beam SPOS Technology

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

A new approach to single-particle optical sizing (SPOS), based on both light-extinction and scattering, using a focused laser beam, quickly counts and sizes protein aggregates from 0.15 to 20 microns, and at much higher concentrations than possible using conventional SPOS sensors. Analysis requires only a relatively small volume (< 1-mL) of protein suspension and does not consume the sample. High sample viscosities resulting from high protein concentrations (>100 mg/mL) can be accommodated.

**ENSURING SAFETY AND EFFICACY OF BIOLOGICS**

2:00 Chairperson’s Remarks

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

**2:05 Structure-based Predictive Modeling of Methionine Oxidation Stability in Proteins**

Vishal C. Nashine, Ph.D., Senior Research Investigator, Drug Product Science & Technology, Bristol-Myers Squibb Co

Oxidation of Methionine (Met) residues in therapeutic proteins may significantly impact their safety and efficacy. Met oxidation may also result in protein aggregation. We describe application of MD simulations towards prediction of the oxidation propensities of Met within several proteins. Our results show that the 2-shell water coordination number (2-SWCN) and simulation averaged solvent accessible area (SAA) are highly predictive of the relative oxidation rates of Met residues.

**2:35 Correlating Monoclonal Antibody Stability with Local Dynamics Using H/D Exchange Mass Spectrometry**

Prakash Manikwar, Ph.D., Scientist I, Formulation Sciences, MedImmune, Inc.

In this study, we investigated how sucrose and arginine impact both the local flexibility and physical stability of an IgG1 mAb. These excipients showed differential effects on conformational stability, storage stability, aggregation rates, and local flexibility of the mAb. New insights and preliminary correlations between local flexibility within specific segments of the CH2 domain and the mAb’s overall physical stability will be provided.

**3:05 Overview of Current Glass Delamination Issues and Implications**

Edward J. Smith, Ph.D., Principal, Packaging Science Resources, LLC

Recently there have been many reports of significant recalls due to particulate matter in vials of drug products due to glass delamination which is a combination of chemical alteration and mechanical failure of the glass surface. This presentation will discuss the types of drugs and vials that present the most risk and review the efforts of glass manufacturers, drug packagers, and standards organizations to assess risk and preclude recalls.

**3:35 Adapting to Biology: Maintaining Container Closure System Compatibility with the Biopharmaceutical Revolution**

Dominick DeGrazio, Associate Scientist, Analytical Laboratory, West Pharmaceutical Services

Alternative measures must be established that aim to preserve the efficacy and functionality of a biologic—from production to patient administration. Sustaining a stable equilibrium for proteins depends upon the ability of container closure systems to maintain compatibility with biological dynamics. Failure of packaging components to adapt can compromise patient safety, drug productivity, and biological stability.

4:05 Close of Conference
This presentation will discuss some of the sources of particle contamination in single-use systems, how to remove them from process equipment, and the impact on the downstream process. The talk will explore various insights in developing and adjusting strategies to manage risks, so that innovation and total cost of ownership benefits can be the focus of the integration.

**ANALYTICS OF SINGLE-USE SYSTEMS**

11:45 PAT Solutions for In-Line and At-Line Analytics from Single-Use Bioreactors
Jens Traenkle, Ph.D., Head, PAT Biotechnology, Bayer Technology Services
Current technologies and new developments for in-line analytics compatible with SUBs will be discussed. Furthermore, in-house single-use solutions from BTS will be presented, which allow automated, extractive sampling from bioprocesses. This technology facilitates the automation of a variety of laboratory analytics, such as metabolites or amino acid panels or even analytics of the biomolecule itself and enables closed-loop control on these parameters. Applications will be presented.

12:15 pm Sponsored Presentation (Opportunity Available)

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

**OVERCOMING SCALABILITY AND DOWNSTREAM PROCESSING CHALLENGES**

2:00 Chairperson’s Remarks
Adam Goldstein, Principal Engineer, Genentech, Inc.

2:05 How to Integrate Single-Use Bioreactors into Vaccine Process Development and Scaling Up?
Sandrine Dessoy, Senior Manager, New Product Development, GlaxoSmithKline
After several years of experience with single use bioreactors, the Cell & Viral Technology department has decided to use disposable bioreactor to enhance the development of the vaccine processes. Single use bioreactor are now fully integrated in the pool of equipment used to perform process development and scaling-up activities. This presentation will highlight the characterization and benchmarking done on these new equipment compared to conventional glass and stainless steel vessels to ensure their right integration in this hybrid equipment platform.

2:35 Scaleable and Continuous Cultivation of Anchorage Dependent Cells in Single-Use Bioreactors: Challenges and Solutions
Brian Lee, Ph.D., President, PBS Biotech
Micro-carrier based suspension culture processes have been used to scale up the anchorage dependent cells in bioreactors. However, the large scale operation, especially in a single use bioreactor, presents its own challenges. In this presentation, a novel single use bioreactor system that enables large scale and continuous cultivation of anchorage dependent cells will be discussed including homogeneous particle suspension, low shear stress mixing, pre-loaded sterile micro-carriers, and an in-situ retention filter device as an enabling technology for these challenges.
Continuous Bioprocessing has been getting more and more attention in the biopharmaceutical industry. Bioprocessing bags, tubing, filters, connectors, etc. are routinely being used at all except the very largest scale across the industry. However, the use of completely disposable processes, especially in the downstream area, is much less common. There are several potential reasons for this, many of which and potential solutions will be discussed during this talk.

CONTINUOUS PROCESSING FOR DOWNSTREAM OPTIMIZATION

4:45 Continuous Antibody Capture Using Countercurrent Tangential Chromatography
Andrew Zydney, Ph.D., Professor and Department Head, Chemical Engineering, The Pennsylvania State University

Countercurrent Tangential Chromatography (CTC) is a new technology that can provide truly continuous product capture and purification using a column-free system that overcomes many limitations of traditional column chromatography. All operations in CTC are conducted on a moving slurry continuously pumped through a cascade of static mixers and hollow fiber membrane modules. Experimental results using a Protein A resin showed good antibody yield, enhanced host cell protein removal, and more than 8-fold greater productivity than a conventional packed column.

5:15 Simulation and Optimization of Continuous Downstream Process in Biopharmaceutical Manufacturing
SeongKyoo Yun, Ph.D., Assistant Professor & Director, Department of Chemical Engineering, Massachusetts Bio Manufacturing Center, University of Massachusetts

Continuous Bioprocessing has been getting more and more attention in the biopharmaceutical industry. A few platforms have been demonstrated in the downstream area, however it is questionable if the configured systems are optimal from the perspective of process economics and facility utilization. This talk will present a study on simulation and optimization of downstream continuous manufacturing. Issues such as media, processing time and quality will be addressed. Pros and cons of the continuous bioprocessing will also be reviewed.
Inaugural
Single-Use Technologies and Continuous Processing in Biopharm Manufacturing
Toward Wide-Scale Implementation of Disposables

11:20 Application of Single-Use Technology in VLP and Nanoparticle Vaccine Production
Jason Li, Ph.D., Sr. Manager, Downstream Process Development, Novavax, Inc.
Novavax's platform combines the flexibility and speed of genetic engineering with the efficiency of single-use disposable technology to produce highly immunogenic nanoparticle vaccines. We are using this nanoparticle platform to develop vaccines against viral, bacterial, and parasitic diseases to address major unmet medical needs to protect against human pathogens. The presentation will discuss the application of single-use technologies in the purification of Respiratory Syncytial Virus (RSV) F protein nanoparticles expressed in baculovirus-Sf9 insect cell culture.

11:50 Sponsored Presentation (Opportunity Available)

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

1:30-2:00 Conference Registration

2:00 BuzZ Session A (Please visit our website for topics)
3:00 Refreshment Break in the Exhibit Hall with Poster Awards
3:45 BuzZ Session B (Please visit our website for topics)

4:45 Close of Conference

4:30-5:00 Short Course Registration
5:00-8:00 Dinner Short Courses (SC8-SC14)
See page 3 for details
Today’s biopharmaceutical manufacturing facilities are smaller, more flexible, efficient and cost-effective, and they are able to adapt quickly to market changes. With modular systems, we could now place an entire small-scale clinical production line inside a manufacturing suite/environment that could be easily scaled up or redeployed elsewhere as needed. We will explore case studies that are in operation today as a proof of concept and technology robustness and the progress made in this area of patient health needs.

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

10:45 Economics of Modular Facility Design and Construction
Howard L. Levine, Ph.D., President, BioProcess Technology Consultants

11:15 Design Considerations for Platform Development: A New Approach to Advance Manufacturing Facility Design
To achieve reductions in schedule, cost and client operating resources as demanded by our clients, our approach was to capture all of our best practices for flexible manufacturing facilities including energy efficiency, modularity, and best value analyses in one place. We will present an overview of our Advanced Design Platform (ADP) and Advanced Manufacturing Platform (AMP) that will help companies develop their own platform and tools to help modify their platform modular concepts to efficiently meet real world conditions.

11:45 Process and Product Considerations for Flexible Manufacturing
Kenneth D. Green, Ph.D., Director, Continuous Improvement, Global Technical Services, Pfizer, Inc.
This talk will discuss desirable product and process characteristics to enable flexible approaches for continuous and multi-product manufacturing. Manufacturing design and operational procedures will be considered and their influence on process platform development.

12:15 pm Flexible and Rapidly Deployed Manufacturing Facilities – Combining Modularization, Standardization and Single Use Strategies
Par Almhem, Co-Founder and President, ModWave LLC.

12:45 Leveraging Development and Process Platforms to Streamline Delivery of Reliable and Flexible Biomanufacturing Processes
Stewart McNaul, Ph.D., Director, Development and Technical Services, Fujifilm Diosynth Biotechnologies
At Fujifilm Diosynth Biotechnologies (FDB) our process platforms are the foundation upon which we build client processes. We will describe how FDB uses process platforms along with standard experimental approaches efficiently to develop processes that are also customized to achieve the best client outcomes. This process design strategy along with our quality systems knowledge promotes effective facility design and sets a standard framework for future manufacturing.

TECHNOLOGY AND PROCESS INNOVATIONS DRIVING FLEXIBLE BIOMANUFACTURING

2:00 Chairperson’s Remarks
Peter Cramer, AIA, Vice President, M+W U.S. Inc. – a Company of the M+W Group

2:05 Innovation Driving Fast & Flexible Development and Manufacturing of Biologics
Jens H. Vogel, Ph.D., Executive Director & Head, Process Science USA, Boehringer Ingelheim
Platform processes have been established for monoclonal antibodies to speed up development and reduce costs. However, in a maturing and
Pipeline 7: MANUFACTURING AND FACILITIES
Inaugural
Flexible Manufacturing of Biopharmaceuticals
Scalarable, Compact, Cost-Effective, Modular and Plastic

increasingly competitive industry, targeted process innovation is again key to more efficiently and sustainability develop diverse biologics portfolios of mAbs and non-mAbs. Examples and data will be shown to illustrate recent and on-going innovations in bioprocess development & manufacturing, such as flexible disposables manufacturing platforms, systemic biology based media platforms, HT analytical tools and continuous processing technologies.

2:35 Panel Discussion and Q&A : Technology and Process Innovations Driving Flexible Biomanufacturing
Moderator: Peter Cramer, AIA, Vice President, M+W U.S. Inc. - a Company of the M+W Group
Panelists: Speakers of the Day

3:05 Combining Single-Use Technologies with Flexible Workforce to Maximize Utilization of Manufacturing
Wolfgang Noe, Ph.D., Vice President, Technical Operations, Agensys Inc.
Use of disposables for manufacturing is becoming a ‘standard’ in the biotech industry. There is a perception that the use of disposables will make each process more economical, however, very often the effective interaction between involved departments during early clinical manufacturing is underestimated. The author will give a detailed insight into the effective manufacturing by using a flexible system where many departments will contribute to the on-time availability of clinical material and the benefit of the start of clinical trials.

3:35 Selected Oral Poster Presentation
Modular Production Systems at the National Center for Therapeutics Manufacturing
Michael Pishko, Ph.D., Director, National Center for Therapeutics Manufacturing, Texas A&M University

3:50 Refreshment Break

4:15 Design, Qualification and Scale-Up to A Disposable Cell Culture Suite to Improve Operational Flexibility
Patrick Sheehy, Ph.D., Associate Director, Pharmaceutical Development, Janssen Biologics Ireland
A case study outlining the approach to design and qualification of a disposable cell culture suite utilizing disposable cell culture bioreactors. This facility will improve product change over times, increase operational flexibility and improve cost efficiency. Further, data from the successful scale-up of cell culture processes from lab scale to disposable cell culture bioreactors will be presented. In addition, data outlining a direct comparison of stainless steel and disposable cell culture bioreactor performance will be discussed.

4:45 Flexible Manufacturing Solutions for the Animal Health Market
Philip Eirod, Scientist, Zoetis
The Animal Health industry responds to many immediate and emergency needs that maintain the security of food supply as well as controlling zoonotic diseases. In order to do this, we not only need reliable manufacturing techniques but they must also be extremely inexpensive by comparison to human vaccine standards, yet generally produced to similar quality standards. This presentation will discuss aspects of process robustness and the challenges of manufacturing in a BSL3 environment.

5:15-6:30 Reception in the Exhibit Hall with Poster Viewing

THURSDAY, JANUARY 16

7:15 am Conference Registration

7:30 Breakfast Presentation (Sponsorship Opportunity Available) or Morning Coffee

INCREASING FLEXIBILITY WITH SINGLE-USE SYSTEMS AND PROCESSES

8:30 Chairperson’s Remarks
Yan-ping Yang, Ph.D., Director, Downstream Purification, Bioprocess Research & Development, Sanofi Pasteur

Yan-ping Yang, Ph.D., Director, Downstream Purification, Bioprocess Research & Development, Sanofi Pasteur
Vaccine development typically takes approximately 12 years from pre-clinical development to licensure, and at a cost of $1 billion. Single use technology and process modeling provides significant opportunities for decreasing capital investment, accelerating development time, and improving overall flexibility of processes and facilities. The presentation will describe specific examples of employing single use technologies and process modeling in the development and manufacture of drug substance, and in the formulation of drug products of vaccine candidates.

9:05 Advantages and Challenges of Single-Use Systems in Biopharmaceutical Development and Manufacturing
John Knighton, MBA, Senior Director, API Large Molecule Technologies & Alliances, Janssen R&D
The use of single use systems continues to grow in the biopharmaceutical industry. The presentation will review the use of single use systems in development and biopharmaceutical manufacturing including a case study from Janssen.

9:35 Selected Oral Poster Presentation
Incorporation of Single-Use Mixing Systems into a Large-Scale Live-Viral Vaccine Upstream Manufacturing Process
Daniel Vellom, Ph.D., Sr. Director, Global Technology Innovation, Sanofi Pasteur Biologics LLC.

9:50 Coffee Break in the Exhibit Hall with Poster Awards

10:05 Evaluating Where Single-Use Technology Provides the Most Value for a Company with a Well Established Manufacturing Infrastructure
Terry Hudson, Ph.D., Associate Director, Process Development Engineering, Genentech, Inc.
The business case for building a flexible facility that heavily leverages single-use technology is well established when manufacturing capacity does not already exist or is insufficient. Are the benefits still the same company with an established, platform based manufacturing infrastructure? What are the primary factors that impact the balance between economy of scale and flexibility? An analysis will be presented to identify where the tipping point lies in such a case.

11:20 Setting Up a Successful Multi-Product Clinical Fill & Finish Operation
Claudia Roth, Ph.D., President, Vetter Development Services USA, Inc.
This case study presents an in-depth review on setting up a clinical manufacturing fill-and-finish operation, and examines how the approach differs from traditional commercial manufacturing, as well as offering solutions that can overcome these difficulties. An important success element is the optimization of disposable technology in material preparation, assembly, compounding, filtration and filling, which helps to resolve many of these challenges and plan for a successful clinical operation.

11:50 Sponsored Presentation (Opportunity Available)

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

1:45 Close of Conference
A system must be well understood when designing Extractable/Leachable (E/L) studies. A lack of industry consensus results in comparing study outcomes. A detailed discussion of the USP Chapters Related to Extractables and Leachables, specifically <661> Plastic Packaging Systems and Their Materials of Construction and <1663> Assessment of Extractables Associated with Pharmaceutical Packaging/Delivery Systems will be presented.

The presentation will discuss the overview of USP strategies for extractables and leachables. The presentation will discuss newly developed and revised USP chapters, appearing in pf 39 (5) September-October 2013, standards related to plastic materials characterization and extractables and leachable testing. It will also discuss other changes in compendial standards related to metal and glass containers.

The evaluation of extractable or leachable hazard begins with compound identification and quantitation. Assessment of risks associated with clinical exposures to these compounds additionally requires consideration of administration route and disposition within the body. The absorption, distribution, metabolism, and elimination (ADME) of identified chemicals frequently differentiate between a hazard and low risk. Risk assessment using this informed approach is essential to accurately define exposure hazards and may eliminate undue follow-on testing.

John Iannone, Program Manager and Technical Specialist, Toxicology, DPD, PDMS, Janssen Research & Development, Pfizer, Inc.


The toxicologist should establish the safety of chemicals originating from the container closure system of a parenteral product. At the extractable stage (i.e. what chemicals might migrate into the drug during storage), the toxicologist should perform a preliminary risk assessment to ensure that there are no serious safety matters identified should these extractables later present as leachables. Subsequently, comprehensive risk assessments are performed on the leachables to ensure patient safety.

Christopher Brynczka, Ph.D., Senior Toxicologist, Toxicology, Gradient Corp.

5:15 ADME Considerations for Risk Assessment of Extractables and Leachables

The evaluation of extractable or leachable hazard begins with compound identification and quantitation. Assessment of risks associated with clinical exposures to these compounds additionally requires consideration of administration route and disposition within the body. The absorption, distribution, metabolism, and elimination (ADME) of identified chemicals frequently differentiate between a hazard and low risk. Risk assessment using this informed approach is essential to accurately define exposure hazards and may eliminate undue follow-on testing.

Christopher Brynczka, Ph.D., Senior Toxicologist, Toxicology, Gradient Corp.

8:30 Chairperson’s Remarks

Pranhitha Reddy, Director, Cell Sciences, BioProcess and Analytical Sciences, Seattle Genetics

5:45 The Toxicological Risk Assessment of Extractables and Leachables: Practices and Procedures to Ensure Patient Safety

The toxicologist should establish the safety of chemicals originating from the container closure system of a parenteral product. At the extractable stage (i.e. what chemicals might migrate into the drug during storage), the toxicologist should perform a preliminary risk assessment to ensure that there are no serious safety matters identified should these extractables later present as leachables. Subsequently, comprehensive risk assessments are performed on the leachables to ensure patient safety.

Christopher Brynczka, Ph.D., Senior Toxicologist, Toxicology, Gradient Corp.

9:35 Leachables from Unexpected Sources

Michael A. Ruberto, Ph.D., President, Material Needs Consulting, LLC

Leachables from Unexpected Sources

Michael A. Ruberto, Ph.D., President, Material Needs Consulting, LLC

3:45 Key Considerations in Designing an Extractable and/or Leachable Study

John Iannone, Program Manager and Technical Specialist, Toxicology, DPD, PDMS, Janssen Research & Development, Pfizer, Inc.

A system must be well understood when designing Extractable/Leachable studies. A lack of industry consensus results in comparing study outcomes with very different study designs, which is cumbersome. This presentation highlights key considerations enabling adequate modeling to examine a system for its E/L profile. Impacting aspects will be outlined and a strategy for designing an E/L study will be presented.

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

Michael A. Ruberto, Ph.D., President, Material Needs Consulting, LLC
The availability of single use and disposable technologies for cell culture processes has enabled the establishment and prevalence of “flexible manufacturing” in upstream areas. This presentation provides case studies on the successful implementation of single use technologies in our platform, and illustrates our investigations and responses to the negative impact of E&L from disposables encountered in upstream processing. Potential constraints in “flexible manufacturing” and risk mitigation strategies that are applicable to cell culture platforms that use disposables in manufacturing will be discussed.

10:05 Selected Oral Poster Presentation: Feasibility of Using Disposable Mixing Systems for Homogenizing Biologic Drug Substance Bulk
Benson Gikanga, Sr. Research Associate, Pharmaceutical Processing and Technology Development, Genentech, Inc.

Protein shear resulting from magnetic coupling of bottom mounted impeller and drive unit via female and male bearing is often observed during drug substance homogenization. Disposable mixing systems incorporating newer and advanced technologies can address this challenge. Mixers evaluated in this study using a monoclonal antibody indicate that levitating impeller technology can offer a better mixing option in terms of particle generation, impact on product quality, and filter fouling during filtration.

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

Gyorgy Vas, Ph.D., Research Fellow, Intertek Pharmaceutical Services

Injectable dosage forms are often stored in a polymer based bags or containers, therefore represent one of the highest risk drug products in relation to the potential introduction of impurities via container closure contact, since any leachable can be rapidly and completely introduced into the patient’s general circulation. The daily doses of those products are often one liter or above, therefore the analytical testing at the SCT level of 0.15 μg/day can be a challenging analytical task. Analytical methods and validation aspects will be presented to analyze the organic and inorganic leachable components at sub-parts-per-billion level.

Case Studies: Impact of E&L from Single-Use Technologies

**Featured Presentation**

11:45 Extractables from Single-Use Bioreactors and Impact on Cell Culture Performance
Yasser Nashed-Samuel, Ph.D., Principal Scientist, Process and Product Development, Amgen, Inc.

Biopharmaceuticals are drugs manufactured by growing genetically engineered cells in bioreactors to produce a therapeutic protein. Plastic single use bioreactors are of interest to biopharmaceutical drug manufacturers due to its significant environmental and cost benefits and flexibility over stainless steel bioreactors. Effect of plastics on the biomanufacturing process is not yet completely understood. A case study on extractables from single use bioreactors and impact on cell culture performance will be presented.

12:15 pm Case Studies on the Impact of Disposables on Cell Culture Processes
Pranthitha Reddy, Director, Cell Sciences, BioProcess and Analytical Sciences, Seattle Genetics

The availability of single use and disposable technologies for cell culture processes has enabled the establishment and prevalence of “flexible manufacturing” in upstream areas. This presentation provides case studies on the successful implementation of single use technologies in our platform, and illustrates our investigations and responses to the negative impact of E&L from disposables encountered in upstream processing. Potential constraints in “flexible manufacturing” and risk mitigation strategies that are applicable to cell culture platforms that use disposables in manufacturing will be discussed.

12:45 Sponsored Presentation (Opportunity Available)

1:15 Luncheon Presentation (Sponsorship Opportunity Available) or Lunch on Your Own
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