Oral Session Descriptions

Session I: **Cell Line Development Advances**
Chairs: **Scott Estes**, Biogen, USA and **Alan Dickson**, University of Manchester, UK

Cell line engineers have a variety of new molecular biology tools at their disposal that significantly expand the realm of options for development of recombinant cell lines or for establishment of host cell lines with new phenotypic traits. As a result, there have been sequential improvements in the speed, efficiency, productivity and product consistency achieved in this space. Recombination-mediated integration has provided one route to improve the speed and consistency of recombinant cell line development. This has been followed by the emergence of precision genome editing tools that have provided unprecedented capabilities to readily manipulate any given genomic loci at the cellular level; both for the purpose of alteration of cellular metabolism to produce a desired growth or product quality attribute, as well as for enabling the precise delivery of genetic payloads to begin the process of engineering recombinant cell lines to produce therapeutic proteins. This session will bring together research presentations that highlight these, and more, recent advances in cell line development with a focus on how the cell line engineering community is tapping into the unprecedented power and flexibility of the genome-editing-technologies.

Session II: **Impact of Process Conditions on Product Quality**
Chairs: **Thomas Ryll**, Immunogen, USA and **Susan Sharfstein**, SUNY Polytechnic Institute, USA

Biopharmaceutical products from cell culture are characterized by their high complexity, particularly post-translational modifications, including glycosylation, carboxylation, and sulfation. Selection and engineering of host cell lines and process conditions can significantly affect these product quality attributes. The ability to manipulate and control product quality attributes, particularly at industrial scale, has received increased attention with the development of biosimilars. This session will focus on elements that govern product quality control through cell line engineering and process parameter optimization for both innovator drug and biosimilar development. Specific focus will be paid to controlling glycan structures and function, and approaches to ensure comparability and/or biosimilarity. Presentations that link process conditions and product quality with underlying cell physiology and metabolism, either experimentally or computationally, are particularly encouraged.

Session III: Advanced Cell Culture Process Controls & Modeling
Chairs: **Michael Butler**, University of Manitoba, CAN and **Raghavan Venkat** MedImmune, USA

This session will cover recent and major achievements in the monitoring and control of cell culture bioprocesses. Advances in process and product analytical technologies to rationally design, control and deliver products with specific quality attributes will be discussed. This will include novel methods of monitoring the growth, metabolism or productivity of the cells during the culture process. The monitoring may involve the rapid analysis of cellular metabolic markers, spectroscopic or electronic changes associated with the state of the culture. The potential of such monitoring to ensure appropriate bioprocess control will be highlighted. In addition, approaches focused on control of cellular metabolism to achieve consistent product quality will be highlighted.

Session IV: Scale-up and scale-down challenges for cell culture-based manufacturing
Chairs: **Frank Chaplen**, Oregon State University, USA and **Anurag Khetan**, Bristol-Myers Squibb, USA

The path to success in large-scale processing in cell culture is not always smooth. Predictability of scale-up is even more critical in an era where manufacturing in a network is becoming the norm. Similarly, having representative scale-down models is imperative for enabling raw material and parameter screening for process characterization, enabling process transfers, and as a troubleshooting tool during the lifecycle of the process. Scale-up and scale-down challenges can result from differences in physical and chemical environment and the associated biological response. Challenges have changed with the evolution of the cell culture platforms and can range from those resulting from differences in kinetics of mixing, from mass transfer challenges due to equipment configuration, to impact of hydrodynamic forces upon process intensification. This session will focus on sharing lessons learned from significant cell culture issues encountered during scale-up and scale-down. We encourage submission of case studies or examples of these types of challenges, particularly as they relate to establishment of sufficient process knowledge in moving towards the goal of planned and predictable scale-up and scale-down to support manufacturing. Presentations may come from, but are not limited to, the following areas: Scale-up, Scale-down, process transfer, facility startup, introduction of at-scale changes and process modeling to improve predictability. Submissions are encouraged from all sectors (industry, academia, and regulatory agencies).

Session V: Integrated Continuous Process Development for Cell Culture
Chairs: **Oscar Lara-Velasco**, GlaxoSmithKline, USA and **Laura A. Palomares**, Instituto de Biotecnología, UNAM, Mexico

Bioprocess engineering advances have resulted in optimized cell lines and traditional processes capable of supplying needed therapeutics to patients. The next frontier for bioprocess engineering is the development of continuous processes where quality is built-in, costs can be reduced, and operations occur in flexible facilities. Integrated continuous processing provides several of these advantages, and demands creative, out-of-the-box, approaches for cell culture and purification operations. In this session, recent advances in integrated continuous processing for biologicals will be explored. Novel approaches to integrate upstream and downstream, analysis of limiting factors for continuous bioprocessing, application of PAT, feasibility case studies, and implementation strategies are strongly encouraged. Presentations describing custom equipment configurations are also welcome in this session.

Session VI: Application of 'Omics and other Technologies for Accelerating and Enhancing Bioprocess Development
Chairs: **Hal S. Alper**, University of Texas at Austin, USA and **Chetan T. Goudar**, Amgen Inc., USA

The performance of mammalian cell culture-based bioprocesses is heavily dependent on the interplay between the host cell, the molecule being expressed and the process conditions employed. Recent technological advances have improved quantification of intracellular interactions and have identified key components related to improved cell performance and process design. This session will focus on recent progress in the development and utilization of cutting-edge tools that are ushering in a new era of cell line and culture process development, in which cell phenotypes, in terms of yield, product quality and consistency, are scientifically accessible and processes are less constrained by risks of changes and less defined by empirical outcomes. This session will highlight how a combination of 'omics, high-throughput process characterization and product analytical technologies are providing insights and

opportunities to drive cell lines and cell culture processes to new levels of performance and control.

Session VII: **Non-Protein Products of Cell Culture Chairs: Bill Miller**, Northwestern University, USA and **Chris Ramsborg**, Juno Therapeutics, USA

The optimization and scale-up of therapeutic protein production is rapidly becoming a mature technology. Rapid advances are being made in the research and development of non-protein products, so there is a compelling need to develop strategies to manufacture non-protein products at large scale, at lower cost, and with greater control. This session will address the potential benefits and market potential of non-protein products, such as engineered T-cells, mesenchymal stem cells, vaccine production for rapidly emerging diseases (e.g., Ebola), directly infused viral vectors, and exosomes. Engineers and scientists working on non-protein products with prior expertise in therapeutic protein production are encouraged to discuss how lessons learned for protein production can be applied to non-protein products, and also highlight where new strategies and technologies need to be developed.

Session VIII: Current Concerns and Emerging Trends in Cell Culture Bioprocessing
Chairs: **Tongtong Wang**, Eli Lilly & Company, USA and **Jamey D. Young**, Vanderbilt University, USA

Since its inception, CCE has provided an important platform for sharing and fostering disruptive innovations (e.g., cell-based therapies) and sustained innovations (e.g., single-use technology and the improvement of recombinant protein titers from 0.1 g/L to 10 g/L) in biomanufacturing. This session is devoted to topics that are innovative, address fundamental concerns underlying the safety and efficacy of biologics, and/or create business value. These emerging topics and technologies often require collaborative efforts among innovators, early technology adopters, and regulatory authorities. Examples of topics include, but are not limited to, next-generation sequencing (NGS), assurance of clonality of production cell lines, prevention and early detection of viral and adventitious agents, approaches to simultaneously optimize productivity and product quality, as well as challenges associated with emerging and more sensitive analytical, bioanalytical, and physical/chemical characterization techniques.

Session IX: Quality by Design and Scale-down Model Qualification
Chairs: **Ashraf Amanullah**, Gilead Sciences, USA and **Robert Thomas**, Loughborough University, UK

The implementation of Quality-by-Design (QbD) approaches for biologics process development and manufacturing is expected to increase process and product understanding and offers potential benefits of an enhanced control strategy, regulatory reporting flexibility and regulatory approval of a design space. Risk assessment strategies, definition of critical quality attributes (CQAs) and design space form the basis of QbD filings. Although such systematic approaches offer the most robust route to a lower risk-optimized process design space, a number of challenges must be addressed. These include the identification of CQAs, and the time and cost of development for executing process characterization/validation studies given the large number of control parameters, critical process attributes, and potentially large number of quality attributes included in the product specification. Statistical models and scaled-down experimental systems can help improve the efficiency of reaching a given design space confidence. We seek abstracts that discuss the application of such approaches to cell culture processes and, in particular, consider advances that improve the efficiency and confidence of

defining the design space via design of experiments and qualification of scale-down models that are representative of the large scale manufacturing process. In addition, critical evaluation and feedback on the value proposition of implementing complex QbD filings versus focusing on a sub-set of elements of QbD is encouraged.

Session X: Novel Protein Formats

Chairs: **John Joly**, Genentech, Inc., USA and **Jennifer Maynard**, University of Texas, USA

Monoclonal antibodies, and in particular monospecific antibodies, comprise a significant fraction of the biologics market able to treat a variety of significant medical needs. Recently, new antibody-based formats have been developed to expand the capabilities and therapeutic effects of these molecules and many of these projects are in clinical development headed for licensure. For instance, numerous bispecific antibodies and those with greater valences have been developed in the last decade to engage multiple therapeutic targets simultaneously. In one instance, this allows for recruitment of T cells to tumor cells by simultaneous engagement of CD3 and a tumor-specific antigen. Other formats allow cytokine targeting to tumor cells by creation of a cytokine-antibody fusion. The scope of this session will include bispecific antibodies and any recombinant protein therapeutic designed for multiple binding specificities or functionalities. Of particular interest will be lessons learned (e.g. minimizing product heterogeneity) during cell line generation and process development for the production of these new molecular entities.