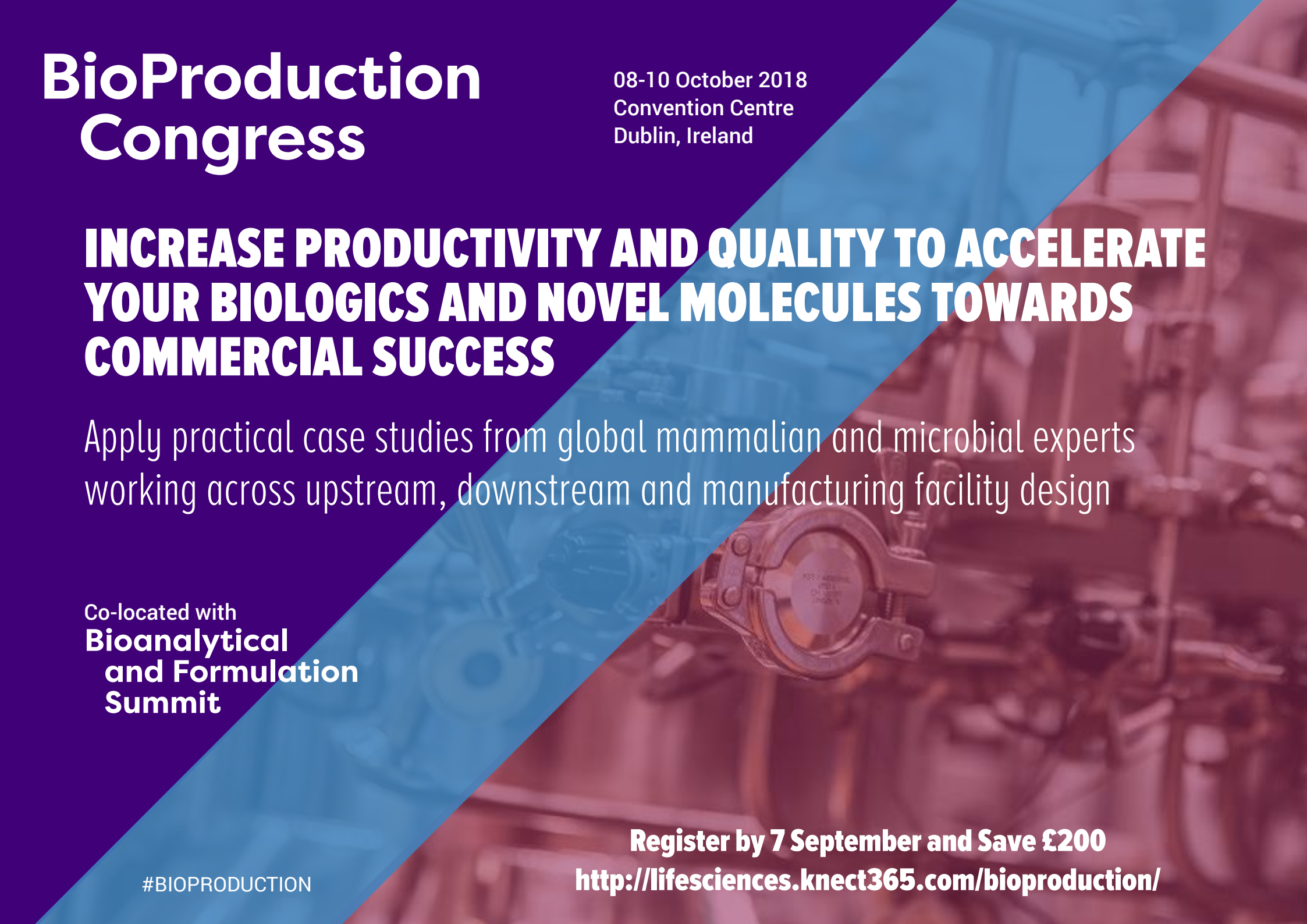
BioProduction Congress

08-10 October 2018
Convention Centre
Dublin, Ireland

INCREASE PRODUCTIVITY AND QUALITY TO ACCELERATE YOUR BIOLOGICS AND NOVEL MOLECULES TOWARDS COMMERCIAL SUCCESS

Apply practical case studies from global mammalian and microbial experts working across upstream, downstream and manufacturing facility design



Co-located with
Bioanalytical and Formulation Summit

#BIOPRODUCTION

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IMPROVE EFFICIENCY ACROSS ALL PHASES OF BIOMANUFACTURING

Upstream Processing

- Hear experiences in applying online control and monitoring to cell culture processes
- Overcome the challenges of upstream production of novel molecules
- Learn how to increase the speed of upstream process development using modelling techniques
- Understand how to improve upstream performance by optimising cell culture media

Manufacturing Strategy & Technology

- Examine next generation facility design to increase capacity, intensity and efficiency
- Adapting biological plants for smaller volume products
- Stay on top of single use standardisation to ensure supply chain security
- Master integrated end to end continuous manufacturing

Downstream Processing

- Catch new case studies on downstream process development
- Discuss alternative capture methods and whether Protein A should be used
- Explore considerations for the capture and purification of novel molecules
- Be informed about the benefits of online monitoring during purification

Microbial Manufacturing

- Discover new approaches to optimise cell harvest and downstream processing
- Tackle production of complex and novel molecules using yeast and E. coli
- Explore the latest online monitoring tools developed for microbial manufacturing
- Uncover how automation, miniaturisation and robotics can accelerate microbial characterisation and validation

Smart Factories

- Delve into strategies to align industry 4.0 and smart manufacturing with biopharma
- Get top tips from industry on digital transformation and smart facility design
- Explore the impact of automation, digital and disruptive technologies: IoT, AI, VR, Smart Sensors, 3D Printing
- Smart data driven decision making in biomanufacturing: Machine Learning, Modelling and Advanced Analytics

THE BRIGHTEST MINDS ACROSS MICROBIAL AND MAMMALIAN BIOPRODUCTION

Eliana Clark,
VP International Manufacturing Operations, Biogen

Aad Van De Leur
COO, Synthon Biopharmaceuticals BV

Thomas Leitch,
VP Vector Manufacturing, bluebird bio

Roman Necina
SVP Process Science & Technical Operations, Shire

PRE-CONFERENCE WORKSHOPS • MONDAY 8 OCTOBER 2018

	BIOANALYTICAL CONGRESS	CELL LINE DEVELOPMENT & ENGINEERING SYMPOSIUM	CONTINUOUS MANUFACTURING	MONITORING AND CONTROL STRATEGY FOR BATCH AND CONTINUOUS BIOPROCESSES
08:15	*Registration*			
09:00	**Chairperson's Opening Remarks** **Christoph Rösli,** Senior Fellow, Late Phase Analytical Development, **Novartis Pharma**	**Chairperson's Opening Remarks**	**Chairperson's Opening Remarks**	**Chairperson's Opening Remarks** **Margit Holzer,** Scientific Director, **Ulysse Consult**
09:10	**Host Cell Proteins Impurities – A Regulatory View** Host cell proteins (HCPs) are process-related impurities which could cause immunogenicity and are therefore considered Critical Quality Attributes. Removal and tight control during the manufacturing process development is required. Specific HCP regulatory guidance is provided by the European Pharmacopoeia and the US Pharmacopoeia. Regulatory decisions based on the interpretation of the regulatory framework will be highlighted. Case studies will be presented to emphasize the regulatory expectations regarding the HCP control strategy. Possible specification limits and the type of HCP assays acceptable during product development and the licensing process will be discussed. **Erika Friedl,** Quality Assessor, **Paul-Ehrlich-Institut,** *Germany*	**Precise and predictable CHO cell line engineering using CRISPR-mediated genome engineering** CHO cells are widely used in the biopharmaceutical industry as a host for production of complex therapeutic proteins. In this regard, efficient genome editing tools to improve CHO cell factories are of great interest. This talk will demonstrate our latest development in genome editing tools, and how the tools in combination with systems biology approaches can pave the way for accelerated generation of desirable CHO cell factories with predicted culture performance. **Lise Marie Grav,** Postdoctoral Researcher, **Technical University of Denmark,** *Denmark*	**Continuous manufacturing** This workshop will provide a comprehensive discussion about the implementation of continuous processing throughout the biomanufacturing lifecycle. From upstream development to downstream development and the interface between the two, this workshop will provide an overview of the various unit operations in which continuous processing is currently being implemented, as well as the challenges of implementation. A review of enabling technologies and lessons learned, along with implementation case studies will be presented.	**Monitoring and Control Strategy for Batch and Continuous Bioprocesses** • Definitions • Regulatory background • Overview of Bioprocess Controls for USP and DSP – What & Why & When to measure & control • Important requirements on process monitoring & control loops – from sampling, measuring, visualization, software, equipment and feed-back or feed-forward controls • Measuring points, frequency, data treatment and storage • Control hierarchies • Routine operation, cleaning, calibration, maintenance • Main differences between batch and continuous bioprocess control **Margit Holzer,** Scientific Director, **Ulysse Consult**
09:40	**Understanding which Critical Quality Attributes to measure** In the last years, an extensive set of putative critical quality attributes has been discussed for antibodies. However, the selection of the correct set of critical quality attributes is crucial during product development as well as for the definition of the control strategy. In this presentation the process to identify project-specific quality attributes, the evaluation of their criticality as well as the selection of critical quality attributes measured during release and stability testing is outlined. **Christoph Rösli,** Senior Fellow, Late Phase Analytical Development, **Novartis Pharma**	**miR-CATCH Identifies Biologically Active miRNA Regulators of the Pro-Survival Gene XIAP, in Chinese Hamster Ovary Cells** imicroRNAs (miRNAs) have demonstrated great potential for the genetic engineering of Chinese hamster ovary (CHO) cells by augmenting cellular phenotypes such as growth rate and culture longevity. A single miRNAs capacity to regulate multiple mRNA targets can be beneficial by controlling entire molecular pathways or devastating by targeting unwanted genes that positively regulate growth or apoptosis, for example. Reliably predicting miRNA targets can be predictably unreliable as the miRNA: mRNA complementarity relationship has been reported to be vastly non-canonical. Here, we used a technique known as miR-CATCH to fish for and identify a panel of bona-fide miRNA regulators of a known pro-CHO engineering candidate, X-linked inhibitor of apoptosis (XIAP). **Paul S. Kelly,** Senior Postdoctoral Research Scientist, **National Institute for Bioprocessing Research and Training,** *Ireland*		
10:10	**Spotlight presentation**	**ChemStress Fingerprinting: A simple, novel platform using small molecules to control and enhance CHO cell factories** The utility of CHO cell factories derives from exploitation of their acquired genetic/functional variation, which enable industry to identify cell lineages with desirable manufacturing properties. Here we discuss novel technologies engineered to provide process control while at the same time enabling optimal leverage of the cell factory using ChemStress fingerprinting. **Jerry Clifford,** COO, **Valitacell**		
10:40	*Morning Coffee*			

	BIOANALYTICAL CONGRESS	CELL LINE DEVELOPMENT & ENGINEERING SYMPOSIUM	CONTINUOUS MANUFACTURING	MONITORING AND CONTROL STRATEGY FORBATCH AND CONTINUOUS BIOPROCESSES
11:20	**NIST Interlaboratory Study on the Glycosylation of NISTmAb, a Monoclonal Antibody Reference Material** **Introduction:** Recently, the production of monoclonal antibodies as biologic drugs has expanded dramatically. Associated with this trend has been a sudden increase in the number of laboratories determining a critical and heterogeneous property of these drugs, namely their glycosylation. This, in turn, has led to a proliferation of analysis methods, including high performance liquid chromatography (HPLC), capillary electrophoresis (CE) and mass spectrometry (MS)-based. The comparability of variety of these methods, especially as they vary lab-to-lab, presents a major challenge in understanding the meaning and accuracy of these measurements. Consequently, an interlaboratory study was conducted by NIST to determine measurement variability in identifying and quantifying N-glycans across laboratories. This work describes results from a recent study on glycosylation analysis of a NIST reference material, NISTmAb, from 73 laboratories worldwide. **Methods:** Each laboratory was asked to perform glycosylation analysis of two monoclonal antibody samples, NISTmAb and a glycan-modified NISTmAb, using their own method. A template was provided to report glycan percent abundances and methods used. Laboratories were asked to create separate reports for each method of analysis. **Results:** To date, 97 reports were submitted by 73 laboratories. Reports came from Europe (41%), North America (37%), Asia (20%), and Australia (2%). Almost half of the reports came from industry (46%), followed by university (33%), research (11%), government (9%), and hospital (1%) laboratories. Comparison of all the techniques will be provided. **Roisin O'Flaherty,** Post Doctorate Research Fellow, **NIBRT**	**Industry perspectives and case studies towards demonstration of monoclonality for biologics manufacture development** In this presentation, we highlight the utility of that imaging technology, describe approaches to verify the validity of those images, and discuss how to present that information within the framework of a biologic filing application. This approach serves as an industry perspective to increased regulatory interest within the scope of monoclonality for mammalian cell culture derived biologics. **Amie Lundquist,** Scientist, **Shire** and **BPOG**	**Continuous manufacturing** This workshop will provide a comprehensive discussion about the implementation of continuous processing throughout the biomanufacturing lifecycle. From upstream development to downstream development and the interface between the two, this workshop will provide an overview of the various unit operations in which continuous processing is currently being implemented, as well as the challenges of implementation. A review of enabling technologies and lessons learned, along with implementation case studies will be presented.	**Monitoring and Control Strategy for Batch and Continuous Bioprocesses** • Case studies • Perfusion monitoring & control strategy • Mab DSP monitoring & control strategy **Margit Holzer,** Scientific Director, **Ulysse Consult**
11:50	**Growing Pains - A Panel Discussion: The challenges and difficulties of developing a biopharmaceutical product from concept to market and methods to help address them** Taking a biopharmaceutical product from concept to market can be a difficult and costly exercise, with the average development cost reported as exceeding $2 billion.1 Any method or measurement which can improve the overall cost of development or reduce the time taken to generate a final product can significantly impact the outcomes of a project. This may include improving product stability, increasing product efficacy, or increasing the reliability of the candidate selection process. In this workshop, Malvern Panalytical has gathered a panel of industry experts to discuss some of the major pain points they have observed in their current workflows. These experts will explain the methods and techniques which they have identified and implemented to overcome these pain points and achieve cost- and time-saving improvements to their development outcomes. **Shahid Uddin,** Head of Formulation, **MedImmune** **Amber Fradkin,** Director, **KBI Biopharma, Inc**	**Isolation of production cell lines with high assurance of clonality and stability** Cell line clonality and stability are the foundation of a robust therapeutic protein production process. Constitutive, high level production of recombinant protein in CHO cells incur metabolic stresses to the cells and consequently often lead to genetic instability. Regeneron has developed cell line technologies for efficient isolation of high titer cell lines that are also stable. In these cell lines antibody genes are expressed in production bioreactors but not in cell expansion and banking process. Here we present studies demonstrating that inducible expression cell lines are more stable than constitutive expression cell lines. **Dipali Deshpande, Ph.D.,** Senior Staff Scientist, Protein Expression Sciences, **Regeneron Pharmaceuticals, Inc**		
12:20		**Spotlight presentation: Assuring and proving monoclonality**		
12:50	*Lunch*			

	BIOANALYTICAL CONGRESS	CELL LINE DEVELOPMENT & ENGINEERING SYMPOSIUM
14:10	**Investigation of Fc Receptor Binding and Pharmacokinetics of Distinct Fc Glycans** Glycosylation of therapeutic proteins is of importance since it can significantly impact biological properties. Glycosylation is heterogeneous and can be subject to batch-to-batch variability. There is a variety of possibilities to influence and investigate glycosylation. In this talk, the in vitro glycoengineering (IVGE) approach will be very briefly introduced and case studies with new data will be presented, including investigation of glyco-modified antibodies incl. changes in galactosylation and sialylation and its impact on Fcγ receptor binding and ADCC activity. Furthermore, new results of a recent study on the impact of certain glycan species on animal PK will be shown. **Marco Thomann,** Senior Scientist, **Roche Diagnostics GmbH**	**Adapting cell line and clone selection methods and workflows for continuous manufacturing**
14:40	**Multi-Attribute Method (MAM) for Process Development and Product Understanding** Biotherapeutics comprise a large portion of pharmaceutical development pipelines. With complex modalities ranging from monoclonal antibodies to gene therapies, better process and product understanding are keys to successful therapeutic development. Quality attribute understanding plays an important role. The complexity of biomolecules leads to a number of assays utilized to study and monitor a wide variety of quality attributes. Recently, a multi-attribute method (MAM) has been developed and implemented in order to simplify analyses. MAM uses liquid chromatography-mass spectrometry (LC-MS) peptide mapping methodology to identify and monitor multiple quality attributes simultaneously in a single assay, as well as impurities. We analyzed method performance through multiple intra-lab studies, and assessed method capability in process development and support. Here we discuss the components of MAM, and present case studies of MAM implementation in a biotherapeutics analytical laboratory. **Carly Daniels, Ph.D.,** Principal Scientist, **Pfizer**	**Incorporation of high-throughput and statistical techniques to advance CHO cell line screening and cell culture development** Recent cell culture strategies are increasing throughput and data volume. Because of this, novel statistical analyses must be implemented to maximize the screening and selection goodness, during the development of production CHO cell lines. In this talk we describe the incorporation of 24-deep-well plates and statistical tools such as multivariate data analysis, data clustering and Design-of-Experiment. The rational adoption of these tools facilitated clone screening and feeding strategies design, and was reasonably predictive of the parameters crucial for process development activities. **Alessandro Mora,** Sr. Scientist, **UMass Lowell**
15:10	**Spotlight presentation**	**Spotlight presentation: Next generation of automation for cell line development**
15:40	*Afternoon Coffee*	
16:10	**How and when do we use equivalence test instead of test for parallelism? And do we?** **Jan Amstrup,** Principal Scientist, **Novo Nordisk**	**Industry case study: Overcoming the challenges of cell line development for difficult to express proteins**
16:40	**Best strategy to evaluate Biosimilars similarity using functional and binding assays.** • Similarity assessment of monoclonal therapeutic drug using functional and binding attributes • Challenges in definition of Critical Quality Attributes (CQA) to determine the Quality Target Product Profile (QTPP) • Statistical approaches to evaluate analytical similarity **Bracha Timan,** Senior Director, Biologics Assays & Technology, **Teva**	**Alternative mammalian cell lines for mAb production** **Dr. Rolf Köhler, PhD,** Group Head CLD1, **Novartis Pharma AG**
17:10	*End of Day*	

MAIN CONFERENCE • TUESDAY 9 OCTOBER 2018

	BIOANALYTICAL CONGRESS	CELL CULTURE & UPSTREAM PROCESS DEVELOPMENT	CONTINUOUS MANUFACTURING
7:50	*Registration*		
9:00		**Chairperson's Opening Remarks** **Tommy Fanning,** Head of Biopharmaceuticals & Food, **IDA**	
9:10	**Method validation based on total error** **Harry Yang,** Senior Director, Head of Statistical Sciences, **Medimmune,** *USA*	**Biomanufacturing facilities of the future** **Eliana Clark,** Vice President, International Manufacturing Operations, **Biogen**	
9:40	**Global regulations for bioanalytical method development and validation** • What are the expectations of the FDA vs. EMA vs. Asian regulators for method development, validation and transfer? • Experiences with meeting global regional regulatory requirements • ICH harmonising requirements • Sharing strategies used to meet expectations **Declan Lowney,** Associate Director**, Janssen**	**Next generation biomanufacturing - Enabling accelerated product development and affordable medicines** Availability of clinical trial material meeting all safety and quality relevant parameters is very often the bottleneck for effective and efficient product development at the same time high costs for routine GMP manufacturing are prohibiting global availability of novel, meaningful therapies. Recently introduced platform approaches, manufacturing technologies, single-use/disposable systems and Process Analytical technology (PAT) have helped to accelerate and de-risk product development and reduce cost of goods (COGS) for commercial products but patient requirements are still not met and affordability of meaningful therapies is still a hurdle for global launches. Digitalisation, automatization, new modalities and novel therapeutic approaches like gene editing and gene therapy are adding complexity but are also offering new opportunities for acceleration of product development and a significant reduction of COGs. **Roman Necina,** SVP Process Science & Technical Operations, **Shire**	
10:10	**Octet® systems get ready for regulated environments - providing data integrity of biomolecule binding responses in real-time and label-free** Biolayer Interferometry (BLI) technology based Octet® systems have been widely adopted in early research, and development of drug candidates and biotherapeutics. Now, with a comprehensive set of tools for compliance, this label-free technology is gaining traction in process development and quality control (QC) labs for concentration analysis in cell culture and purification, for kinetic and potency analysis of drug-target and drug-Fc receptor interactions, and for stability analysis by assessing changes in activity in stressed and forced degradation samples. Discover the go-to solution providing versatility and flexibility necessary in development combined with rigor and simplicity needed in a QC environment. **Philip Buckle,** Senior Scientist, **Pall FortéBio, UK**	**Next generation biomanufacturing and facility implementation: Technical advances in manufacturing technologies to improve process productivity**	
10:40	*Morning Coffee*		
11:20	**Demystifying the USP Chapters on Bioassay Development and Analysis** USP Chapter <1032>, Design and Development of Bioassay provides a framework for bioassay development, though many of the statistical concepts are not implemented from lack of understanding. This talk will cover the use of different statistical designs and analysis for developing a bioassay that is robust. **Steven L. Walfish,** Principal Scientist and Standards Liaison, **USP**	**Multivariate analysis of perfusion process data: Insights on process control strategies with respect to product quality** Multivariate analysis (MVA) is a statistical approach frequently used to generate meaningful information from the vast amount of data recorded from mammalian cell culture. However, the application of MVA is not straightforward, since there are a multitude of approaches and methods that can be used. Here, a novel framework is presented to gain valuable insight on perfusion bioreactor control strategies and how these influence product quality and productivity. Firstly, two-way hierarchical clustering is applied to the process data. This analysis enables the isolation of the intervals that present, statistically, the highest and lowest correlation with process performance indicators (specific productivity, product titre and cumulative daily productivity). For these intervals, the process variables which correlate with the highest and lowest overall productivity are identified and evaluated. The results are subsequently cross-validated using partial least squares (PLS) regression and pairwise correlations. The same workflow is applied for process intervals with high and low product quality. By comparing and contrasting the variables in the two aforementioned workflows, a shortlist of variables is provided that allows to define process control strategies to increase bioreactor productivity, without impacting product quality. **Sarantos Kyriakopoulos,** MSAT Scientist, Cell Culture, **BioMarin International**	

MAIN CONFERENCE • TUESDAY 9 OCTOBER 2018

	DOWNSTREAM PROCESSING	MANUFACTURING STRATEGY & TECHNOLOGY	SMART FACTORIES	MICROBIAL MANUFACTURING
7:50	*Registration*			
9:00	**Chairperson's Opening Remarks** **Tommy Fanning,** Head of Biopharmaceuticals & Food, **IDA**			
9:10	**Biomanufacturing facilities of the future** **Eliana Clark,** Vice President, International Manufacturing Operations, **Biogen**			
9:40	**Next generation biomanufacturing - Enabling accelerated product development and affordable medicines** Availability of clinical trial material meeting all safety and quality relevant parameters is very often the bottleneck for effective and efficient product development at the same time high costs for routine GMP manufacturing are prohibiting global availability of novel, meaningful therapies. Recently introduced platform approaches, manufacturing technologies, single-use/disposable systems and Process Analytical technology (PAT) have helped to accelerate and de-risk product development and reduce cost of goods (COGS) for commercial products but patient requirements are still not met and affordability of meaningful therapies is still a hurdle for global launches. Digitalisation, automatization, new modalities and novel therapeutic approaches like gene editing and gene therapy are adding complexity but are also offering new opportunities for acceleration of product development and a significant reduction of COGs. **Roman Necina,** SVP Process Science & Technical Operations, **Shire**			
10:10	**Next generation biomanufacturing and facility implementation: Technical advances in manufacturing technologies to improve process productivity**			
10:40	*Morning Coffee*			
11:20	**Protein A comparability and a path to dual sourcing** As the bioprocess industry matures, many therapies are coming to market with alternative purification strategies as defined by standardised platform processes. A common factor for all Fc based therapies is the use of Protein A chromatography resins for their resolving power and efficiency compared to non-affinity based processes. Several new resin manufacturers have developed hydroxide stable protein A resins to compete with the established vendors. This has driven suppliers to evolve current offerings in terms of stability, productivity and price. Additional drivers in the industry also require increased security of supply and marketing authorisation holders want operational flexibility to manage inventory and reduce cost. In this presentation we will address the comparability between Protein A resins on three test molecules to compare key characteristics that could create a plug and play resin environment where dual sourcing of resins could become a reality. We will also highlight strategies for implementing this approach within the product lifecycle where clinical forethought can support long term operating success. **Aled Charles,** R&D Manager, Purification Process Sciences, **MedImmune**	**Strategies for aligning Industry 4.0 and a smart manufacturing vision with biopharmaceutical production** • Smart Manufacturing Vision: What is needed to align industry 4.0 and smart manufacturing within the biopharmaceutical sector? • Sensor development to handle harsh chemical environments • Connectivity: How to reduce waste by connecting all devices in manufacturing? • New process platforms, increased intensity for different cell modalities • Adapting batch originated biopharmaceutical manufacturing with smart manufacturing vision – Implementing continuous manufacturing for highly autonomous smart facility • Applicability of robotics, automation and software platforms in biopharmaceutical manufacturing environment • People and digital environment - Identifying the right workforce skill set required for digitalisation and where people are needed in automated field? • How can 3D printing be part of disposable processes? • Regulatory expectations and requirements for smart factories in the biopharmaceutical sector **John Levesley,** Senior Process Engineer, **PM Group**		**Thought leader's discussion panel: Where is, microbial production going?** • Where is, microbial production going? • Where do we see microbial hosts in the bioproduction space? • What technologies could change the market for microbial production? • What technologies and product advances are driving industry away from traditional CHO platforms? • Advantages, recent improvements and advances of microbial expression – yeast and E. coli • Microbial vs. Mammalian Expression: • Titres and Volumes • Impurity levels • Process timeframes • Product quality • Scalability • Cost of Goods/ Production • Feasibility for integrated end to end continuous biomanufacturing • Developing platform approaches

	BIOANALYTICAL CONGRESS	CELL CULTURE & UPSTREAM PROCESS DEVELOPMENT	CONTINUOUS MANUFACTURING
11:50	**The use of sensitivity analysis to set acceptance criteria in the validation of biological assays** In biomarker diagnostic work, an analyte assay may lead to a binary or qualitative outcome such as disease or not-disease, or to-treat or not-to-treat. It is important to know what level of random change in the analytes can be tolerated to guarantee the claimed diagnostic performance. We can define the maximum allowable deviation (MAD) such that the binary endpoint claim is maintained. It can be determined from previously run validation datasets by varying analyte signals in small increments and then creating ruggedness plots. These can then be used to set acceptance limits for validation studies of operational factors. For multi-analyte assays this is not entirely straightforward, but summary measures including logistic regression scores make it possible. It still remains to confirm if such limits are achievable given the underlying variability of the analytes. An accelerated stability example is presented. **Graham Healey,** Senior Biostatistician, **Oncimmune**	**Development of Perfusion Scale-Down Models for Medium Development** Due to the complex nature of bioreactor medium, high through-put scale-down models that simulate the perfusion bioreactor system while supporting large multivariate design of experiment approaches are necessary. For that purpose, two models were developed, optimized, and applied for perfusion medium development. With this first-generation perfusion medium, a cell line developed for fed-batch application achieved over 3-fold increase in productivity. **Amy Johnson,** Associate Director, Cell Culture & Media Development, **Regeneron Pharmaceuticals Inc.**	
12:20	**Interlaboratory Performance Metrics from the MAM Consortium New Peak Detection Round Robin Study** **Richard Rogers,** Principal Scientist, **Just Biotherapeutics,** *USA*	**Spotlight presentation: A representative from CMC**	
12:50	*Lunch & Live Labs*		

	DOWNSTREAM PROCESSING	MANUFACTURING STRATEGY & TECHNOLOGY	SMART FACTORIES	MICROBIAL MANUFACTURING
11:50	**Process development considerations for novel highly potent recombinant proteins** Botulinum neurotoxin is effective in the treatment of several movement disorders. Native BoNT/A is comprised of a family of highly related neurotoxins produced by Clostridium botulinum bacteria and BoNT/A (subtype A1) is notable as the strain used to produce the commercial products such as abobotulinumtoxinA (Dysport).An increased understanding of the structure-function relationship of BoNT provides an opportunity to engineer recombinant (r) BoNTs with unique pharmacologic properties and therapeutic applications. This presentation will describe the challenges and opportunities associated with Process Development and GMP manufacture for rBoNT products **David Gruber,** Head of Downstream Process Development, **Ipsen Biopharm**	**Case study Bioplant (UCB, Switzerland), our e-plant setup and future roadmap** The Bioplant built in 2013-2015 at the UCB, Bulle site (Switzerland) aimed to be a paperless plant. In order to achieve this many digital systems were put into place and interfaced to each other. As part of our continuous improvement process, other systems/interfaces have been added or are planned. Our e-plant setup and roadmap covers for example: manufacturing control, sampling data management, process data management, scheduling, equipment management. **Anna Marya Jobe,** Project Lead, BioPlant Operations, **UCB Farchim SA**		**Online monitoring of protein refolding** The need for diversity and flexibility in process development is constantly increasing in the biopharmaceutical industry. Working with microbial expression systems offers low cost and high yield production of non-glycosylated proteins. Exogenous proteins expressed in E. coli are often difficult to produce in other cell types and frequently lead to the formation of inclusion bodies in the bacteria. Although IBs represent an easy-to-harvest source of highly pure recombinant proteins, they are associated with complex purification processes including protein refolding. The complexity relies in the lack of reliable assay to examine the structural steady-state of the target protein. Currently, the most consistent approach to show refolding includes a capture step to evaluate the chromatographic performance of the refolded product. The scale up of refolding as a unit operation can also prove to be a challenging task. Here, we will discuss strategies to monitor the structural changes of a model protein using online sensors. **Dr Cécile Brocard,** Director Downstream Development, Biopharma Process Science, **Boehringer Ingelheim RCV GmbH & Co KG**
12:20	**Demystifying Extractable Testing** With single-use technology now at the forefront of existing new and upcoming biopharmaceutical manufacturing processes, the industry is finding that it is playing catch-up with regards to the characterization of single use components through extractable testing. Different approaches to testing have emerged in guidelines from organizations such as BPOG, USP and BPSA but how can the end-user confidently assess and mitigate risk when vendor extractable data is confusing and difficult to compare? **Graeme Proctor,** Product Manager, Single-Use Technologies, **Parker Bioscience Division,** *UK*	**Spotlight presentation: A representative from Asahi**	**Manufacturing strategy: Designing a Next Generation "Smart" Biomanufacturing Facility** In the biopharmaceutical industry "time to market" is a major driver. An aspect of recent technology development which has shown promise to help address this driver is the use of flexible, single-use manufacturing solutions. These solutions not only decrease or eliminate entirely the time required for production equipment preparation and cleaning, but also significantly decrease the capital investment required for construction of new production plants. IN addition with the adoption of intensified processing further significant productivity gains can be made. During this webinar the design of a state-of-the-art bioproduction plant based on the use of single-use systems throughout the manufacturing process will be described. Particular emphasis will be placed on the flexibility of single-use systems. This will also be explained from the point of view of the contract manufacturing organisation Abzena Overseeing all of these systems is the automation that enables modern process equipment to be operated efficiently in a controlled manner. Sartorius' approach to automation & analytics with the comprehensive implementation of the Umetrics suite within Abzena's facilities and how it has been adopted at Abzena will also be described. **Miriam Monge,** Global Head of mAb/intesified Market Segment, **Sartorius Stedim Biotech** **Dr. Jim Mills,** Senior VP of Technical Operations, **Abzena**	**Latest advancements in producing difficult to express proteins in E. coli** Full length recombinant antibodies represent one of the fastest growing classes of biopharmaceuticals. The downside is that the manufacturing of these antibodies is expensive, requires extensive production times and yield relatively low product as they are currently made on mammalian cells. Batavia's SCOPETM microbial fermentation technology is a novel platform for highly controlled regulation of protein expression and high yields in E. coli. This technology allows very cost-effective manufacturing processes for proteins or antibody fragments, which does not require glycosylation. We will present our latest data for the production of a functional scFv antibody fragment. **Sagrario Arias Rivas,** Program Manager & Scientific Liaison, **Batavia Biosciences**
12:50	*Lunch & Live Labs*			

	BIOANALYTICAL CONGRESS	CELL CULTURE & UPSTREAM PROCESS DEVELOPMENT	CONTINUOUS MANUFACTURING
14:10	**Implementing bioassays for a kλ-Body** **Anaëlle Dos Santos,** Head of Bioanalytics Unit, **Novimmune**	**Understanding cell culture media variability** • Role of trace elements in cell culture performance and product quality • How cofactors, lipids, vitamins, etc. affect quality attributes • Information about new media that is available **Dr. Rui Oliveira,** Associate Professor, **FCT/UNL**	**Digital transformation and smart biomanufacturing facilities: Case study from Boehringer Ingelheim** **Samet Yildirim,** Manager, Technology & Innovation, Global Technology Management, **Boehringer Ingelheim Fremont, Inc.**
14:40	**High-throughput Release N-glycan Method for Product Quality Assessment** N-Glycosylation of biotherapeutics is an important critical quality attribute. Glycans can influence protein stability, serum clearance, immunogenicity and pharmacokinetics. Therefore it is crucial to monitor the full glycan profile of a glycoprotein throughout discovery, clinical and manufacturing phases. A High-throughput RapifluorMS N-glycan method has been employed in our lab to address the challenges that are encountered with product quality support and meet aggressive timelines. This presentation will provide an overview of the development workflow to automate all the steps from sample preparation to data analysis of the RapifluorMS released N-glycan analysis. **Vithiya Vimalraj,** Senior Scientist, **GlaxoSmithKline,** *UK*	**Using fluorescence spectroscopy for the analysis of raw material and cell culture media variability** Fluorescence excitation-emission matrix (EEM) spectroscopy offers unique possibilities for the quantitative and qualitative analysis of nearly all types of cell culture media used in the manufacture of biopharmaceuticals. EEM measurements produce a unique molecular fingerprint for complex biogenic mixtures such as cell culture media that contain multiple fluorophores (e.g. tyrosine, tryptophan, riboflavin, etc.). EEM spectra of cell culture media are very sensitive to compositional change, degradation, and improper sample handling. These effects can be easily identified and quantified using multivariate analysis techniques (chemometrics). In Galway we have been developing the use of EEM-chemometrics to rapidly and robustly analyse all the various types of cell culture media encountered during manufacturing including raw materials, cell culture media, bioreactor broths, and proteins. We will illustrate the efficacy of this approach by presenting a wide range of case studies including the analysis of hydrolysate variance, chemically defined media photodamage, variance analysis of basal and feed media, and the analysis of media preparation and filtration methods. This methodology is suitable for all media types, can also be applied to macromolecule characterisation, and has low capital and unit test costs, making it an ideal PAT tool for bioproduction. **Alan Ryder,** Principal Investigator - Nanoscale Biophotonics, **NUI Galway**	**Large Scale Single Use Bulk Drug Substance Freeze and Thaw Platform** This presentation is an overview of a novel single use end to end solution for freeze, thaw, handling, and transportation of Bulk Drug Substance. It will touch on topics like points of design consideration, scalability, stability, and proof of concept. **Thomas Hilfer,** Senior Scientist, Biologics Engineering, **MSD,** *USA*
15:10	**Using a data driven approach to improve biomanufacturing processes** • The industry is challenged to improve its manufacturing process robustness and reduce the costs associated with limited process understanding; • An increasing range of technical advances becomes available to improve process efficiency; • The application of sophisticated PAT tools in combination with multivariate data analytics has a high impact on commercial processing; • This presentation gives an insight on how data driven approaches can help to evaluate technological advances to improve production processes. A representative from **Sartorius**	**Spotlight presentation**	
15:40	*Afternoon Coffee*		

MAIN CONFERENCE • TUESDAY 9 OCTOBER 2018

	DOWNSTREAM PROCESSING	MANUFACTURING STRATEGY & TECHNOLOGY	SMART FACTORIES	MICROBIAL MANUFACTURING
14:10	**Alternative capture methods for mAbs: crystallisation, flocculation, precipitation, etc.** **Alois Jungbauer,** Professor, **University of Natural Resources and Life Sciences Vienna**	**Digital transformation and smart biomanufacturing facilities: Case study from Boehringer Ingelheim** **Samet Yildirim,** Manager, Technology & Innovation, Global Technology Management, **Boehringer Ingelheim Fremont, Inc.**		**Downstream challenges with highly hydrophobic proteins: A case study** We will present challenges encountered during the downstream process development for a highly hydrophobic protein expressed as inclusion bodies. Conventional DSP techniques using aqueous buffer systems failed due to limited protein solubility and poor recovery from chromatographic media. While RPC proofed suitable for the capture step, the 2nd orthogonal purification step required a rather unusual cation exchange chromatography with a solvent background. **Dr Christian Eichmueller,** Head Downstream Process Development, Bioprocess Developmement Kundl, **Sandoz GmbH**
14:40	**Innovative Purification Techniques and Downstream Process Development for Next Generation Therapeutics** **David O'Connell,** Lecturer in Biotherapeutics, School of Biomolecular & Biomedical Science at University College Dublin, Ireland, **University College Dublin**	**Large Scale Single Use Bulk Drug Substance Freeze and Thaw Platform** This presentation is an overview of a novel single use end to end solution for freeze, thaw, handling, and transportation of Bulk Drug Substance. It will touch on topics like points of design consideration, scalability, stability, and proof of concept. **Thomas Hilfer,** Senior Scientist, Biologics Engineering, **MSD,** *USA*	**Case study: BPOG Digital Plant Maturity Model** (awaiting final confirmation)	**How to purify Fabs from "dirty" E. coli cell lysates?** Nowadays the use of microbial expression systems for the production of antibody fragments instead of mammalian cell culture is getting increasingly important. The possibility to produce these highly important proteins by use of "simple" organisms provides several advantages, especially in upstream processing, e.g. short cultivation times as well as high expression rates. However, in most cases subsequent downstream processing of these proteins still represents the main challenge on the way to the final product. Since microbial systems generally do not excrete recombinantly produced proteins, they have to be purified from crude cell lysates after high pressure homogenization. Unfortunately, these lysates do not only contain the desired proteins, but mainly impurities, such as HCPs, DNA and lipids, which cause complications in the purification of the target protein. In my talk, I will show how we tackled this challenge and purified a Fab from E. coli crude cell lysate using different chromatography-based strategies. We developed and investigated an affinity-based as well as a non-affinity-based Fab purification strategy which we compared regarding purification performance (product purity and product recovery) as well as the necessity of pre-treatment of the crude cell lysate for purification. Summarizing, you will learn different possibilities of how to purify a high-value antibody fragment from a "dirty" E. coli crude cell lysate. **Thomas Gundinger,** PhD Student, **TU Wien**
15:10	**Chromatographic Clarification as a Tool to Remove Problematic Host Cell Proteins** **Dr. Hani El-Sabbahy,** Application Engineering Specialist, **3M,** *UK*	**Spotlight presentation: A representative from Sartorius**	**Spotlight presentation: A representative from BioProduction Group**	**Value adding microbial-based solutions for the GMP-production of recombinant proteins** Wacker Biotech, known as THE MICROBIAL CDMO, handles several GMP production sites in Europe with capacities to deliver multiple hundred grams of drug substance per batch. We will present case studies for our innovative and cost-saving E. coli technologies for the production of difficult-to-make biopharmaceuticals. Our approach to process design and problem solving enables our customers to meet their challenging timelines during clinical development as well as to match their needs by reaching the commercial phase. **Guido Seidel,** Managing Director Operations, **Wacker Biotech (Operations)**
15:40	*Afternoon Coffee*			

	BIOANALYTICAL CONGRESS	CELL CULTURE & UPSTREAM PROCESS DEVELOPMENT	CONTINUOUS MANUFACTURING
16:10	**Biotherapeutics Formulation Design in the Age of Lab Automation and Biological Performance Screening** • An overlook of the evolution of our automation line addressing scientific as well as data handling matters. **Kathrin Schäker-Theobald,** Senior Scientist I, NBE HTS Operation & Analytics, **AbbVie Deutschland**	**Case Study: Reduction of copper in cell culture media during scale up from 1L to 12000L** **Dr.Jan Bechmann,** Associate Director in Cell Culture Process Development, **Boehringer Ingelheim Pharma GmbH & Co. KG**	
16:40	**Round-Table Discussion: Automating analytical workflows** • Future focuses • Data analysis and evaluation strategies • Moving away or moving on to alternatives • Strategies to implement automation into existing workflows **Mario Richter,** Principal Scientist DMPK-BA, **AbbVie Deutschland GmbH & Co. KG**	**Characterisation of a perfusion-based vaccine production process** Janssen Vaccines has recently moved towards late stage development and hence characterized its vaccine manufacturing process. The robustness of the perfusion-based process to produce the vaccine at the targeted quality has been demonstrated using Quality by Design (QbD) and a science and risk-based approach. In this talk, we present how the manufacturing process was characterized at Janssen Vaccines. The presentation focuses on the upstream process characterization: from the criticality assessment through the definition of Proven Acceptable Ranges for each critical USP parameter, including the use of a reduced-scale model. **Perrine Rouel,** Upstream Processing Scientist, **Janssen Vaccines,** *The Netherlands*	**Case Study: Continuous connected downstream processing** **Gorazd Hribar,** Project Manager**, nextBioPharmDSP, Lek**

	DOWNSTREAM PROCESSING	MANUFACTURING STRATEGY & TECHNOLOGY	SMART FACTORIES	MICROBIAL MANUFACTURING
16:10	**Alternatives to Protein A for the capture of Fc-containing bispecific antibodies** Bispecific antibodies (BsAb) are an important new class of protein therapeutics. BsAb are designed to recognize and bind to two different antigens, often for the purpose of retargeting immune effector cells to kill cancer cells. Currently two BsAb are approved as therapeutics by EMA and one by FDA. Using UniRatTM human heavy chain antibody technology, we have produced several BsAb, each targeting a tumor antigen and CD3. Our lead BsAb are monoclonal IgG4 antibodies engineered in the CH2 and hinge domains to silence Fc-function and prevent arm exchange, respectively. The molecules comprise 3 chains, two non-identical human heavy chains—one full length, the other derived from the UniRatTM and lacking the CH1 domain. The third is a human kappa light chain bound to the full-length heavy chain. Correct pairing of heavy chains is achieved through knobs-into-holes technology. For this and many BsAb, the use of Protein A for capture is problematic due to the presence of Fc-containing product variants in the crude BsAb mixture. In designing a manufacturing process for BsAb, alternative Fc affinity methods for capture were investigated and a suitable alternative was found. Properties and performance characteristics of alternative capture methods will be discussed. **Steven Chamow,** Principal, **Chamow & Associates, Inc.**	**Hybrid facilities: Case study on the integration of stainless steel and disposables** **Ron Bates,** Director, **Bristol-Myers Squibb**	**Digital and disruptive technologies in biomanufacturing - Merging classical engineering with smart algorithms** • What is a factory in 4.0 looking like? • What type of new technologies companies investing in e.g. new reactors, new sensors, new setups of how factories are build e.g. flexible. • What is an optimal way to start digitalisation? • Do you need to replace all old technologies? • How to in bed smart technologies into classical systems? • What technology and hardware can be made smart in traditional biomanufacturing factory? • Future of hardware – Bedding in smart algorithms into technologies	**Industry case study: Design and validation of scale down models for process characterisation in microbial manufacturing**
16:40	**Case Study: Continuous connected downstream processing** **Gorazd Hribar,** Project Manager**, nextBioPharmDSP, Lek**	**Managing variability and scalability in single use facilities** • How to deal with scalability in biomanufacturing? • How large can you go using single use bioreactors? • Linking stainless steel and single use systems for scalable solutions • Managing rapid scale up of biomanufacturing • Managing variability in biomanufacturing using single use systems **Justyna Adamczyk,** Senior Technology Transfer and Process Validation Specialist, **Polpharma** **Adriana Kędzierska-Mencfeld,** Head of Production Department, **Polpharma Biologics**	**Towards bioprocess digitalisation through smart supervisory control based on Raman spectroscopy** Within the last years, we elaborated a digitalization platform for bioprocesses in direct collaboration with leading companies for process digitalization, advanced monitoring sensors and cell cultures (Siemens, Kaiser Optical Systems and Merck). The implementation facilitates the handling of process wide information, gained by classical sensors and modern process analyzers like Raman spectroscopy, implemented in upstream and downstream. Furthermore, the platform enables the integration of several developed digital solutions for the analysis, modeling, interpretation, monitoring and control of bioprocesses, embedded in a holistic framework. Those digital solutions are based on advanced engineering statistics, machine learning as well as deterministic approaches, combined in a new generation of models- hybrid bioprocess models. The obtained results demonstrate the high flexibility of statistical models combined with the robustness of deterministic models, leading to a significant reduction of required experiments, while showing a decent prediction accuracy. Moreover, the tools were integrated into the process development workflow in several collaboration projects with the biopharmaceutical industry. **Alessandro Butte,** Senior Scientist and Lecturer, **ETH Zurich**	**Automation and miniaturisation of a microbial fermentation platform for the production of antibody fragments** The benefits of automating and miniaturising our Microbial fermentation process development work include reducing our process development timelines by increasing our throughput and making better use of available resources. This presentation will discuss how the two systems recently implemented in our lab (namely the Ambr250 Modular system from Sartorius and the Freedom Evo 200 from Tecan) are being used to aid our evaluation of process performance and product quality as well as considering future challenges. **Geoff Brown,** Principal Scientist, Upstream Process Sciences, **UCB**

	BIOANALYTICAL CONGRESS	CELL CULTURE & UPSTREAM PROCESS DEVELOPMENT	CONTINUOUS MANUFACTURING
17:10	*End of Day Two*	**Providing high biosimilarity by harnessing the analytical technologies during upstream development** Consistent high-quality antibody production is a main goal for biosimilar mAb manufacturing. Process variables have high effect on products' quality in different ways. Here, two case studies are discussed to understand how critical process parameters affect the N-glycan structure of a mAb. To understand the clonal and molecule effects on the N-glycosylation behaviors, two different CHO-M cell clones, producing stable TNF alpha and VEGF blocker monoclonal antibodies, were cultivated in 3-L bioreactors. The impact of feeding strategies, cultivation temperature, culture pH and galactose addition were investigated on glycan pattern and cell behavior in bioreactors. The results showed that temperature effects on G0F-GN and G0F may vary depending on the molecule even the same cell line was used. On the other side, pH had significant effects on fucosylated complexes in both molecules. In order to provide the high biosimilarity in terms of glycosylation and charge variant profiles, process conditions were optimized for both molecules using a variety of different strategies. After providing the high biosimilarity in 3 L bioreactors, a successful scale-up strategy was applied to 200 L GMP production by keeping the products' quality in critical quality attributes. **Duygu Ayyildiz Tamiş,** Head of Process Development, **Turgut Pharmaceuticals**	**Advanced Control using Process Analytics for Purification and Particle Engineering** The development of continuous downstream manufacturing processes is not without its challenges: whether it is finding continuous processing solutions to batch unit operations that are 'inherently controllable'; designing real-time analytics that can provide timely information of a sufficient quality; or control systems that can handle the complexity. This presentation discusses continuous processing alternatives to chromatography and lyophilisation in DSP - two die-hard batch unit operations - and how we might go about creating automation capable of six sigma levels of control. **Dylan Jones,** Development Lead, **Sanofi**
17:40	**Rosetta - Philae and Hayabusa 2 - MASCOT: Long Term Space Projects with Landers** **Stephan Ulamec,** Philae Project Manager, **German Aerospace Center,** *Germany*		
18:25	*End of Day Two and Evening Entertainment*		

	DOWNSTREAM PROCESSING	MANUFACTURING STRATEGY & TECHNOLOGY	SMART FACTORIES	MICROBIAL MANUFACTURING
17:10	**Advanced Control using Process Analytics for Purification and Particle Engineering** The development of continuous downstream manufacturing processes is not without its challenges: whether it is finding continuous processing solutions to batch unit operations that are 'inherently controllable'; designing real-time analytics that can provide timely information of a sufficient quality; or control systems that can handle the complexity. This presentation discusses continuous processing alternatives to chromatography and lyophilisation in DSP - two die-hard batch unit operations - and how we might go about creating automation capable of six sigma levels of control. **Dylan Jones,** Development Lead, **Sanofi**	**The challenges of building high containment facilities** Ipsen Biopharm have invested significantly in the design and build of a state of the art containment suite for the development and manufacture of future pipeline products. This talk will highlight the challenges to overcome when delivering such specialist facilities. **Barry Stevenson,** Facilities and Technical Support Manager, BioPharmaceutical Development, **Ipsen Biopharm**	**Utilisation of AI and IOT in data driven biopharmaceutical manufacturing decision making** • How does the IOT and 4.0 direct better decisions? • Smart biomanufacturing using data driven decisions from IOT • Utilisation of AI systems and process development and supply chain data to aid data driven decision making	**Assembling toolboxes, platform technologies and defining workflows for high throughput process development** **Marco Oldiges,** Head of Bioprocesses and Bioanalytical Group, **Forschungszentrum Jülich GmbH**
17:40	**Rosetta - Philae and Hayabusa 2 - MASCOT: Long Term Space Projects with Landers** **Stephan Ulamec,** Philae Project Manager, **German Aerospace Center,** *Germany*			
18:25	*End of Day Two and Evening Entertainment*			

MAIN CONFERENCE • WEDNESDAY 10 OCTOBER 2018

	BIOANALYTICAL CONGRESS	CELL CULTURE & UPSTREAM PROCESS DEVELOPMENT	DOWNSTREAM PROCESSING
8:50	**Chairperson's Remarks** **Patrick Sheehy,** Scientific Director, **Janssen**	**Chairperson's Remarks**	
9:00	**Bispecific antibodies – key process and analytical challenges** **Patrick Sheehy,** Scientific Director, **Janssen,** *Ireland*	**Adapting biomanufacturing strategies and technologies for next generation therapies** **Thomas Leitch,** Vice President, Vector Manufacturing, **bluebird bio**	
9:30	**How innovation of drugs shapes modern bioanalysis and potency assessment – The rise of ATMPs and the challenge of appropriate assays** Innovation is a pivotal process in drug development to address unmet medical needs. Advanced therapy medicinal products (ATMPs) are amongst these innovations and the number of ATMPs entering clinical stages has been substantially increasing over the last few years. Bioanalysis and potency assessment has proven to be a challenge, as the mode of action for cellular therapeutics is often not fully characterized. Currently most companies apply a multi-assay approach, often consisting of cellular surface analysis, cytokine release and one form of functional cell-based assay. The challenge arises when these assays need to be validated. While walking you through some case studies, we will address these assay and regulatory challenges and how they can be handled. **Melody Sauerborn,** Trainer and Independent Consultant, **Scientia Potentia Consultancy**	**Adapting biomanufacturing strategies and technologies for next generation therapies** With the introduction of new innovative high potent biopharmaceuticals like Antibody Drug Conjugates (ADCs) the industry had to adapt and move to complete different strategies to produce these products. Next to the standard cGMP requirements additional safety aspects need to be taken into account. In addition, the volumes of these products would be limited resulting in smaller facilities and options to utilize single use materials but also the need to adapt certain equipment. In this talk I will present how Synthon Biopharmaceuticals approached these challenges resulting in in-house manufacturing capabilities. **Aad Van De Leur,** Chief Operations Officer, **Synthon Biopharmaceuticals BV**	
10:00	**Spotlight session**	**Smart biomanufacturing facilities of the future - A Representative from IDBS**	
10:30	*Morning Coffee*		
11:10	**Analytical assay development for CAR T cell characterization** **Eric Alonzo,** Scientist, Cellular Analytics, **Bluebird Bio,** *USA*	**Process robustness using Quality by Design driven approaches** Cell culture processes seem to be established but still lack of thorough understanding in reaching higher titers and process robustness using process technological means. This contribution show different aspects of Quality by Design driven approaches for • Identification of the limiting amino acid using PAT and automated modelling approaches • Model based experimental designs for targeting maximum information content of the experiment for a given objective, such as media titer optimization or lactate uptake • Scale down model establishment to analyze the effect of large scale in homogeneities. We want to provide a methodological toolset which should be used as a development for established but also novel products. **Christoph Herwig,** Professor for Bioprocess Engineering, **Vienna University of Technology**	**Late stage development and control strategy for monoclonals** The control strategy is in the biopharmaceutical industry an integral part of the QbD paradigm used within Upstream and Downstream Processing. In Downstream Processing control can be achieved in multiple ways. At Synthon advanced automation is combined with a disposable materials approach. Selective testing is used to further exercise control. In this presentation two Downstream Processing examples will be given, describing control strategies for both monoclonal antibody and antibody drug conjugates, which both have their specific demands. **Bas Kokke,** Principal Scientist, **Synthon**

	MANUFACTURING STRATEGY & TECHNOLOGY	SMART FACTORIES	MICROBIAL MANUFACTURING
8:50	**Chairperson's Remarks**		
9:00	**Adapting biomanufacturing strategies and technologies for next generation therapies** **Thomas Leitch,** Vice President, Vector Manufacturing, **bluebird bio**		
9:30	**Adapting biomanufacturing strategies and technologies for next generation therapies** With the introduction of new innovative high potent biopharmaceuticals like Antibody Drug Conjugates (ADCs) the industry had to adapt and move to complete different strategies to produce these products. Next to the standard cGMP requirements additional safety aspects need to be taken into account. In addition, the volumes of these products would be limited resulting in smaller facilities and options to utilize single use materials but also the need to adapt certain equipment. In this talk I will present how Synthon Biopharmaceuticals approached these challenges resulting in in-house manufacturing capabilities. **Aad Van De Leur,** Chief Operations Officer, **Synthon Biopharmaceuticals BV**		
10:00	**Smart biomanufacturing facilities of the future - A Representative from IDBS**		
10:30	*Morning Coffee*		
11:10	**Thought Leaders Discussion: Steps towards standardisation and interchangeability to ensure single use systems supply chain security** • Steps towards the standardisation of single use technologies e.g. standardised geometrics and connectors • Interchangeability and improving connectivity of single use systems • Ensuring supply chain security for critical equipment and single use components in commercial manufacturing • How to improve company internal organisation to ensue supply chain security • Interactions between vendors and pharma companies • Addressing the future challenges and equipment demands in the industry today	**Hybrid modelling: Beyond purely data driven approaches for efficient knowledge management in industry 4.0** At the moment, the (bio)pharmaceutical industry is adopting high-throughput technologies to investigate process conditions, recording the data in dedicated data-bases. Artificial Intelligence (AI), data science and big data approaches are being promoted to exploit the data and describe the complex systems. While for some cases this might proof possible, even with high-throughput experimentation it will be infeasible to study the impact of the combinations of all possible changes in the process and/or organisms experimentally (referred to as the curse of dimensionality), wherefore the application of the data-driven approaches is overall only of limited use. To overcome this problem knowledge from first-principles, biology, physics, which is freely available and generally valid, can be integrated along with data-driven approaches, reducing the complexity of the modeling problem at hand. The application of such an approach, referred to as hybrid modeling, to a controlled drug release case is presented and the learnings from the development of this model are shared. **Moritz von Stosch,** Senior Manager Fermentation, **GlaxoSmithKline**	**Continuous harvesting of secreted products from a high cell density perfusion bioreactor of Pichia Pastoris** We have developed a novel harvesting device, BioSettler, to settle the microbial yeast cells from the harvest stream and return the settled cells to high cell density perfusion bioreactor. We demonstrate this continuous harvesting application for BioSettler on a 1.5 liter high cell density perfusion bioreactor of yeast Pichia pastoris cells, overexpressing and secreting a natural sweetener protein Brazzein. **Dhinakar Kompala,** Founder & CEO, **Sudhin Biopharma Company**

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	BIOANALYTICAL CONGRESS	CELL CULTURE & UPSTREAM PROCESS DEVELOPMENT	DOWNSTREAM PROCESSING
11:40	**Immunogenicity • and what about the targets?** A short introduction about T-cell independent ADA response and multimeric targets (TNFα and IL-17) followed by a case study based on COVA322, a dual TNFα and IL-17A inhibitor that went into a FIH SAD Psoriasis Study stopped due to the observed safety profile **Clara Albani,** Research Associate, **Covagen**	**On-line and Off-line monitoring of CHO cell health in a bioreactor to allow for early identification of cell death** Monitoring and maintenance of cell health in a bioprocess is crucial with regards to both the productivity of the cells and to the overall quality of the final product. Traditional approaches involve sampling and off-line testing of cell viability using dye exclusion at fixed points throughout the process. By utilising the novel methods of on-line digital holography and impedance flow cytometry we can provide a more complete picture of cell health during a bioreactor run, allowing for informed intervention at potential critical points in the process. Such methods compare well with off-line methods of conventional flow cytometry and dye exclusion. These methods not only provide a more in depth look at the stage of cell death but also analyse the population on a single cell basis thus providing an insight into the cell population dynamics, which might otherwise be masked in the bulk population. Such methods can lead to potentially greater yields of the desired product. **Adam Bergin,** Ph.D. Student, **NIBRT**	**Online Monitoring of product quantity, purity and potency during chromatographic purification** Currently, regulatory agencies encourage pharmaceutical industry to implement QbD approaches into manufacturing processes. We integrated additional online sensors for monitoring of loading and elution during into a conventional chromatography workstation. By mathematical correlation of offline data on quantity, purity and potency to the obtained online data predictive models have been established. These generated models enable controlled loading and peak cutting based on defined quality settings. Time and labour intense offline analytics are only needed for the model set-up not during the process. Batch to batch variations are detected in real time and batch failure can be reduced by real time process control. **Dominik Sauer,** Ph.D. Student, **University of Natural Resources and Life Sciences, Vienna**
12:10	**A Smart Microfluidic Technology for Early Discovery and Analytics** Protein purity analysis by microfluidic separation offers distinct advantages over traditional capillary electrophoresis in sample consumption, ease of use, and speed of analysis. Using a smart microfluidic platform for high throughput quantitation and quality screening of proteins. The method utilizes a microchip which utilizes real-time electro-hydrodynamic optimization to eliminate variability in reported results, i.e. run-to-run and day-to-day variability, which may be caused by micro-scale fluctuations in the physical properties of chips, reagents, or instrument components. **Anubhav Tripathi, Ph.D.,** Professor, Bioengineering and Medical Science, **Brown University,** *USA*	**Spotlight Session – A representative from ABEC**	**Productivity opportunities in downstream commercial processes** Two case studies will be presented to show productivity opportunities undergone at Roche to standardize processes and reduce waste. Improvement of the endotoxin control process validation strategy and global alignment on vent filter integrity testing. Both projects were implemented to the Drug Substance manufacturing network, reducing resources and costs. **Albin Simoni,** Senior Process Engineer Global MSAT, **Roche**
12:40	*Lunch*		
13:30	*Poster Tour*		

	MANUFACTURING STRATEGY & TECHNOLOGY	SMART FACTORIES	MICROBIAL MANUFACTURING
11:40	**Data driven approaches for performance optimisation of commercial DS manufacturing** In this presentation, we demonstrate how scientific and data-driven approaches were used to improve process performance and consistency of a commercial mAb within established/registered manufacturing process ranges. For the cell culture process, a multivariate data investigation identified an interaction effect between two manually-driven parameters contributing to variability in USP titre and quality attributes For protein purification, value stream/process flow mapping identified numerous opportunities to reduce wastes (non-processed material) at various unit operations. Realisation of these opportunities was approached in a non-regulatory impactful way (working within existing ranges) to reduce post-approval change management to a minimum. The combined effect of these changes has resulted in an increase in 10% final DS quantity at minimal additional manufacturing cost and disruption (to implement the changes) to manufacturing operations. The key role of creating and maintaining good process databases and the application of appropriate analytics tools as key enablers for process changes (and the need for further investment here) will be discussed. **Francisca Gouveia,** Senior Process Expert, **Novartis**	**Data driven approaches for performance optimisation of commercial DS manufacturing** In this presentation, we demonstrate how scientific and data-driven approaches were used to improve process performance and consistency of a commercial mAb within established/registered manufacturing process ranges. For the cell culture process, a multivariate data investigation identified an interaction effect between two manually-driven parameters contributing to variability in USP titre and quality attributes For protein purification, value stream/process flow mapping identified numerous opportunities to reduce wastes (non-processed material) at various unit operations. Realisation of these opportunities was approached in a non-regulatory impactful way (working within existing ranges) to reduce post-approval change management to a minimum. The combined effect of these changes has resulted in an increase in 10% final DS quantity at minimal additional manufacturing cost and disruption (to implement the changes) to manufacturing operations. The key role of creating and maintaining good process databases and the application of appropriate analytics tools as key enablers for process changes (and the need for further investment here) will be discussed **Francisca Gouveia,** Senior Process Expert, **Novartis**	**Application of Computational Fluid Dynamics (CFD) in biopharmaceutical industry: Increasing scale-up insight and directing optimisation of equipment** The demand for complex therapeutic proteins, plasmids and antibodies for treatment of various diseases has increased continuously in the last decades, prompting the continuous development of new production processes. These complex molecules can only be produced via cell cultivation of under controlled parameters in a reactor. These fermentation processes are performed in small scale during development and early clinical phases (e.g. 5 • 200 L). Only in later clinical phases and during market supply the full production scale is utilized (e.g. 4000L). These processes are also transferred between sites in order to cope with additional market demand. So all production processes undergo scale-up and transfer steps that have the potential to significantly impact quality parameters or business performance. In microbial fermentation the main transfer and scaling parameters are volumetric, however there are some significant differences if equipment is scaled up only volumetrically. The experience of the many successfully performed process scale-ups and transfers shows that procedures are well understood. Still the additional usage of computational fluid dynamics (CFD) is advisable, and it can assist in risk mitigation upfront and reduce time during root cause analysis. Calculating the reactor specific energy demand of our equipment, looking at shear rates and turbulence parameters, can identify anomalies or local extremes that can be addressed. This makes CFD a powerful tool in optimizing geometries as well as in finding suitable operating conditions in pharmaceutical production processes. In this case CFD simulations with ANSYS Fluent were generated for a 20L Pilot-scale fermenter in the development area and a 4000L Large Scale Manufacturing fermenter. Both simulations were verified via mixing times in situ, and subsequently several output parameters were compared. Differences can be identified, that have a potential to impact the production process. With the aim to continuously reduce the gap between development and production scale, several equipment setups were designed. CFD with ANSYS Fluent was used to evaluate agitator set ups in terms of physical and functional properties. Interestingly, no solution approximates to the production scale in all studied aspects. Based on a wide experience of process scale-up, the parameters were ranked according to the relevance for process performance and we propose a path forward toward a more robust scale up. **Christian Sam,** Process Science Austria Fermentation Scientist, **Boehringer Ingelheim RCV GmbH & Co KG**
12:10	**Managing raw materials and auxiliary components supply with in-time delivery and release to enable continuous manufacturing** Various market drivers such as increase range of therapeutic molecules beyond monoclonal antibodies, personalized medicine, making therapy options available to broader affected population and improving patient outcome while managing cost to patients, forcing biopharmaceutical industry to look beyond traditional discovery to development to manufacturing options. The manufacturing process innovation that lead to increase in flexibility while decreasing overall drug product cost can help meeting some of the market challenges. A lot of progress has been made to improve upstream to downstream unit operations. However, many challenges need to overcome to implement well-functioning fully integrated continuous manufacturing. Typical biologic manufacturing consumes hundreds of raw materials including media, supplements, process chemicals, filters, resins, and excipients. Managing of flow of these components and releasing them on a timely basis is a daunting task without either increasing inventory levels or implementing non-traditional approach to receive release and use these materials while meeting all quality requirements. In this presentation we will present available technologies and discuss various options with risk and benefit analysis to overcome some of these challenges. **Nandu Deorkar,** Vice President R&D Biopharma, **Avantor**	**Spotlight presentation: Managing data integrity, transferability, privacy and cyber security risks implied by Industry 4.0**	**Spotlight presentation: Feedback from CMO's: tech transfer strategies and setting specifications for microbial production** • Expectations from industry for tech transfer of microbial based processes: Document and criteria required • How do CMOs handle intermediates, refolded proteins and final drug products? • Dealing with the differences from mammalian production • Scaling up strategies for commercial production using microbial processes
12:40	*Lunch*		
	Poster Tour		

	BIOANALYTICAL CONGRESS	CELL CULTURE & UPSTREAM PROCESS DEVELOPMENT	DOWNSTREAM PROCESSING
14:00	**The analytical toolbox for viral vector characterisation: progress and challenges** The field of gene therapy through the use of viral vectors has advanced rapidly in recent years with an increasing number of clinical programs moving towards market approval. As advances are made in this area there is the need for an analytical toolbox to enable rigorous characterisation of viral vectors to demonstrate purity, potency, stability and safety. In addition, the analytics to support process development for manufacture of viral vectors must be in place to ensure clinical demands can be met for different products and higher vector quantities per product. Current analytical methods for viral vector characterisation will be discussed as well as some of the challenges faced in process development and characterisation of the expanding potential commercial product pipeline. **Clare Trippett,** Senior Bioanalytical Scientist, **Centre for Process Innovation**	**Innovative Dynamic Control of Upstream Processes using Soft sensors and Predictive Metabolic Modeling Approaches for Therapeutic Protein Development 2.0** Therapeutic proteins development becomes more challenging due to the complexity of the diverse molecule formats. In-depth characterization of high producer cell lines and bioprocesses is essential to ensure robust and consistent production of recombinant therapeutic proteins in high quantity and quality for clinical applications. Controlling the environmental stress present during the cultivation of cells is a key for the successful production of an intended bio-therapeutic protein. Process development and in particular the use of high throughput systems required sampling for controlling. One of the most important parameter is the cell growth, but sampling, sample dilution and analyzing is time consuming and generates high efforts in the case of high throughput fermentation systems. Sampling allows also only a look in the culture status at a certain time point, the information between two sample points is missing. Therefore we develop a new soft sensor, which takes online signals of the bioreactor, which are correlated to cell growth to estimate the cell growth. The new approach based on multiple linear regression and on artificial neural network processed the common online signals of the bioreactors to estimate the cell growth as online signal during cultivation time. The captured data is applied in a metabolic network model for the analysis of intracellular metabolic fluxes of Roche's working horse of therapeutic protein production - the Chinese Hamster Ovary cell. The generated metabolic information and prediction has the potential to set a new standard for efficient and innovative process development and process control bridging from research to market. In conclusion, the combination of quantitative metabolite profiling, multivariate data analysis, and mechanistic network model simulations can identify metabolic traits characteristic of high-performance clones and empowers the scientists to develop efficient processes. New approach in metabolic/process modeling/controlling and results will be presented. **Wolfgang Paul,** Senior Scientist, Group Leader Cell Culture Research, **Roche Diagnostics**	**Supporting the Biopharmaceutical Industry through Innovations in Downstream Purification** CPI supports the UK biopharmaceutical industry by engaging in a variety of collaborative work programmes to support process innovation and facilitate the development and adoption of new manufacturing and analytical technologies. Case studies will be presented from a number of collaborative projects looking to improve downstream operation through formulation innovation, the development of automated continuous purification, the development of a platform for virus production and prediction of performance characteristics to improve the efficiency of manufacturing systems for future targets. **Stuart Jamieson,** Senior Downstream Scientist, **Centre for Process Innovation**
14:30	**Anisotropy Resolved Multi-dimensional Emission Spectroscopy (ARMES) for the analysis of proteins in solution** The use of intrinsic fluorescence spectroscopy for the analysis of protein structure, stability, and aggregation has significant benefits in terms of sensitivity and minimal unwanted perturbation. However, most fluorescence-based assays use either single point measurements or two-dimensional spectra both of which have poor information content. The situation is further complicated by the presence of multiple-fluorophores in most therapeutic proteins (e.g. IgG > 100 fluorophores…) which makes spectral interpretation difficult because of extensive spectral overlap. To facilitate detailed structural analysis of multi-fluorophore proteins, Anisotropy Resolved Multi-Dimensional Emission Spectroscopy (ARMES) can be used to extract more information from a single fast measurement. ARMES is a 4D measurement (λex×λem×If×r) in which the anisotropy (r) measurement can provide information about both structural and physicochemical changes and aggregation of proteins. This novel method also involves the use and development of multivariate analysis tools to extract the most useful information from the 4D measurements which can be implemented using standard benchtop spectrometers. Here we present some of the latest ARMES developments for the characterisation of proteins with case studies involving Insulin, IgG, and albumin type proteins. **Alan Ryder,** Principal Investigator, **NUI Galway**	**Case study on upstream processing from Allergan** **Martin Bond, Allergan Biologics Ltd., an affiliate of Allergan plc**	**Validation of next gen depth filter technology in a commercial downstream process** **Kim Hermans,** Team Lead MSAT Purification, **Sanofi**

	MANUFACTURING STRATEGY & TECHNOLOGY	SMART FACTORIES	MICROBIAL MANUFACTURING
14:00	**Regulatory Feedback: GMP inspections** **Dearbhla Cullen,** Inspector, **Health Products Regulatory Authority (HPRA)**	**Innovative Dynamic Control of Upstream Processes using Soft sensors and Predictive Metabolic Modeling Approaches for Therapeutic Protein Development 2.0** Therapeutic proteins development becomes more challenging due to the complexity of the diverse molecule formats. In-depth characterization of high producer cell lines and bioprocesses is essential to ensure robust and consistent production of recombinant therapeutic proteins in high quantity and quality for clinical applications. Controlling the environmental stress present during the cultivation of cells is a key for the successful production of an intended bio-therapeutic protein. Process development and in particular the use of high throughput systems required sampling for controlling. One of the most important parameter is the cell growth, but sampling, sample dilution and analyzing is time consuming and generates high efforts in the case of high throughput fermentation systems. Sampling allows also only a look in the culture status at a certain time point, the information between two sample points is missing. Therefore we develop a new soft sensor, which takes online signals of the bioreactor, which are correlated to cell growth to estimate the cell growth. The new approach based on multiple linear regression and on artificial neural network processed the common online signals of the bioreactors to estimate the cell growth as online signal during cultivation time. The captured data is applied in a metabolic network model for the analysis of intracellular metabolic fluxes of Roche's working horse of therapeutic protein production - the Chinese Hamster Ovary cell. The generated metabolic information and prediction has the potential to set a new standard for efficient and innovative process development and process control bridging from research to market. In conclusion, the combination of quantitative metabolite profiling, multivariate data analysis, and mechanistic network model simulations can identify metabolic traits characteristic of high-performance clones and empowers the scientists to develop efficient processes. New approach in metabolic/process modeling/controlling and results will be presented. **Wolfgang Paul,** Cell Culture Research, **Roche Diagnostics**	**Production of fabs in E. Coli – A comparison of expression systems** In my talk, I will compare different E. coli expression platforms for the production of Fabs and discuss their advantages and challenges to be tackled. **Oliver Spadiut,** Assoc. Prof.; Integrated Bioprocess Development, **TU Wien**
14:30	**Optimising process fit to enhance annualised productivity** Tech Transfer between facilities presents a business opportunity to enhance productivity and optimise facility fit whilst minimising impact on process performance and reliable supply. This presentation presents a case study of an intra-site tech transfer of a commercially approved platform biologics process. An overview of the productivity opportunities evaluated, the risk based approach to implementation and tech transfer outcomes are provided. **Cillian McCabe**, Team Leader, Technical Services/Manufacturing Sciences, **Eli Lilly and Company**	**Mastering the digitalization challenge in bioprocessing through smart data analytics and modeling** Throughout the past years, we elaborated several digital solutions based on advanced engineering statistics, machine learning and deterministic approaches for the analysis, modeling and interpretation of bioprocesses. Furthermore, we integrated them into the process development workflow in several collaboration projects with the biopharmaceutical industry. This presentation will show the possibilities to accelerate development and reduce risks in bioprocessing through digital engineering solutions, and will outline key technology and business drivers to master the digital transformation challenge in bioprocessing. **Michael Sokolov,** Postdoctoral Fellow and Lecturer, **ETH**	**Development of a high yielding E. coli periplasmic Fab production platform** **Mark Ellis,** Principal Scientist, **UCB**

	BIOANALYTICAL & FORMULATION	CELL CULTURE & UPSTREAM PROCESS DEVELOPMENT	DOWNSTREAM PROCESSING
15:00	**Spotlight session**	**Accelerated media and feed development through use of media and feed library screening** Simplifying and accelerating upstream process development is a must for biotech firms. We found that effective collaborations with specialized media development companies is paramount. Menarini Biotech and BD developed a medium/feed platform for particularly challenging CHO DG44 cell lines. Through this program, we evaluated 20 proprietary chemically defined media and six feeds. The best combination resulted in four-fold performance increase in less than three months. **Noemi Moroni,** Upstream Scientist, **Menarini Biotech,** *Italy*	**Chromassette®: A stackable, single-use chromatography cassette enabling next-generation bioprocessing** A stackable, single-use and pre-packed chromatography cassette with a supported bed, Chromassette® is a novel product concept in DSP, addressing the current key challenges in manufacturing. Chromassette combines the separation capabilities of chromatography resins with the convenience of a pre-packed, modular cassette as shown in a range of application examples. **Gerald Platteau,** Senior Application Engineer, **JSR Life Sciences**
15:30	*Afternoon Coffee*		
16:00	**Measuring Protein Assembly at High Concentration** The self-assembly and aggregation of proteins can lead to the formation of protein assemblies with sizes ranging from nanometres to micrometres. For several biologic formulations, protein concentrations in excess of 150mg/ml are required. Analysis of size heterogeneity at high protein concentrations presents an analytical challenge. I will discuss methods we use for aggregation analysis at protein concentrations up to 200mg/ml. **Jennifer McManus, Head of Department of Chemistry, Maynooth University**	**Assessing the potential of a 24-well miniature bioreactor system as scale-down model for mammalian cell culture processes** The need to bring new biopharmaceutical products to market more quickly and to reduce final manufacturing costs is driving early stage, small scale bioprocess development. This presentation will cover the engineering characterisation of a single-use 24-well parallel miniature bioreactor (MBR) in terms of power input, liquid phase mixing and oxygen mass transfer. The robustness of the MBR will be demonstrated with regard to the reproducibility of 24 parallel fed-batch CHO cultivations. Examples will be given for the application of this MBR to characterise and rationally scale cell culture processes. **Frank Baganz,** Senior Lecturer, **University College London**	**Development and validation of high throughput scale down purification models** **Andrea Rayat,** Senior Enterprise Fellow in Bioprocessing, **University College London**
16:30	**Biophysical characterization of HexaBody®-based IgG antibodies: The impact of formulation** The HexaBody® format is a novel platform for the potentiation of therapeutic antibodies by enhancement of antigen-dependent hexamer formation at the cell surface, which may drive subsequent target receptor activation or complement activation. The biophysical characteristics and stability of HexaBody-based model compounds in different formulations will be discussed, probed by a variety of analytical techniques. **Muriel van Kampen,** Senior Scientist, **Genmab**	**Faster process development via hybrid modeling and intensified Design of Experiments** In this contribution, an intensified Design of Experiment (iDoE) methodology will be introduced. The iDoE approach is based on the idea that the values of certain factors do not need to be kept constant throughout the experiments. Instead the value of the factors can be changed during the experiments, e.g. after a specified time a step-change from 23 to 30 (°C) can be applied in temperature. In this way a classical Design of Experiment plan can in principle be executed using less experiments. The iDoE method is applied to industrial and simulated E.coli fed-batch fermentations. A dynamic hybrid modeling method is adopted for the analysis of the data, since the analysis cannot be accomplished with the traditional static statistical methods. The process understanding gathered from the iDoE is compared to DoE results. The results suggest that the number of experiments can be reduced by a factor of three to two, meaning less than half of the experiments of a classical DoE are required with the iDoE method. In addition, the understanding of the process dynamics is much improved, which is of particular importance to assess the impact of temporal deviations in the factors on the process response. It also seems possible to integrate the process development activities better with the development of the process control strategy. **Moritz von Stosch,** Senior Manager Fermentation, **GlaxoSmithKline**	**Evaluating the impact of mixing during viral inactivation and neutralization post protein A chromatography using small scale mixing models** In a typical downstream purification process, mAbs and Fc-fusion proteins are exposed to acidic conditions during elution from affinity resins and during viral inactivation. It is well known that acidic pH and high ionic strength can promote formation of nonnative protein structures, thereby resulting in aggregation. pH adjustments of the solution generally require a mixing process that can have a potential impact on formation of aggregates and necessitates the requirement of a scale down model to study its impact. However, developing scale down models for mixing during viral inactivation poses a number of challenges due to the number of factors impacting the process. Mixing models need to account for the engineering principles governing mixing scale down, as well as shear parameters. In addition, mixing models should account for the addition rates of acid/ base during the process and location of the addition ports and pH electrodes within the vessel. The above parameters can impact the product through generation of high molecular weight species as well as process related impurities through precipitation of host cell proteins. This case study looks into the impact of mixing speed and acid/base addition rates on process performance and generation/ reduction of process related impurities. **Maike Juergens,** Purification Scientist, **Bristol-Myers Squibb**

	MANUFACTURING STRATEGY & TECHNOLOGY	SMART FACTORIES	MICROBIAL MANUFACTURING
15:00	**Applications of handheld Raman Truscan RM in biopharmaceutical manufacturing** Raman spectroscopy, a vibrational spectroscopy with a number of useful properties (non-destructive, non-contact, robustness) has significant potential benefits in biopharmaceutical manufacturing. Raman spectroscopy offers intrinsically high molecular selectivity, the ability to measure in water, no (or minimal) sample preparation, and flexible sampling options. From its inception, our handheld Raman spectrometer, TruScan RM, has provided small molecule manufacturing 100% raw materials inspection without prohibitive financial or staffing investments. Now TruScan RM has evolved with the addition of TruTools, an on-board chemometric software package which expands raw material identification applications to complex material analysis problems such as materials with similar chemical compound structures, at-line process checks, and final product identification. Here we present a few examples of how Truscan RM and TruTools can be used in biopharmaceutical manufacturing for raw material analysis (Amino acids, Cell Culture media and buffers), at-line monitoring of fermentation, and final product identification of therapeutic proteins. **Shailesh Karavadra,** Technical Sales Manager, **ThermoScientific**	**Spotlight presentation**	**Spotlight presentation: Microbial plant design: engineering of large scale facilities** • Microbial plant design – how to reduce bottlenecks in microbial production in facility design • New developments in facilities for E. coli manufacturing • Evaluating single use bioreactors and modular facilities for microbial manufacturing • Trends towards smaller systems and localised production for microbial platforms
15:30	*Afternoon Coffee*		
16:00	**Control of antibody glycosylation during the upstream or downstream stages of a bioprocess** Glycan profiles of monoclonal antibodies produced in cellular bioprocesses are dependent upon the enzymic activities present in the host cell line as well as the growth conditions during the bioprocess. The glycosylation profile can be controlled during upstream processing by cell engineering or media manipulation during cell growth. An alternative approach is by enzymic remodelling during downstream processing. The relative value of each of these possible strategies will be evaluated for the production of an antibody. **Michael Butler,** Chief Scientific Officer (CSO), **National Institute of Bioprocessing Research & Training (NIBRT),** *Ireland*	**Building Industry 4.0 and smart manufacturing into the supply chain for data driven logistics: Real time release, predictive maintenance and raw materials monitoring** • Connectivity tracking • Blockchain and raw material quality tracking • Sensors and analytics enabling real time release • Development of sensors to make raw material data accessible to whole supply chain • Connectivity to reduce time of release of raw materials in GMP environment • Real time release of product • Automated re-ordering of raw material supplies • Smart factories and data driven logistics/supply chain	**Reinventing a legacy process for the 21st century: A case study on implementing a single-use bioreactor in an anthrax vaccine fermentation process** This talk presents the factors considered in the development of a modern but comparable anthrax vaccine fermentation process to a legacy counterpart. It highlights the approach of using data gathered from a legacy process to design a new operating space. Also, the role of how a single-use rocked bioreactor was used to achieve this transformation will be discussed. **Williams Olughu,** Senior Scientist, **Porton Biopharma Limited**
16:30	**Strategies towards the development of holistic manufacturing control strategy** • Industry integration of diagnostics metrics and systems to track process behaviour and process capability: Understanding how well your processes are doing? • How IT links to Pharma 4.0 and enables smarter project and operational execution • Development of preventive measures as well as detection methods • Steps towards the development of a holistic approach for biomanufacturing control • Best practices from other industries **Julian Morris,** Technical Director, **University of Strathclyde**		**Faster process development via hybrid modeling and intensified Design of Experiments** In this contribution, an intensified Design of Experiment (iDoE) methodology will be introduced. The iDoE approach is based on the idea that the values of certain factors do not need to be kept constant throughout the experiments. Instead the value of the factors can be changed during the experiments, e.g. after a specified time a step-change from 23 to 30 (°C) can be applied in temperature. In this way a classical Design of Experiment plan can in principle be executed using less experiments. The iDoE method is applied to industrial and simulated E.coli fed-batch fermentations. A dynamic hybrid modeling method is adopted for the analysis of the data, since the analysis cannot be accomplished with the traditional static statistical methods. The process understanding gathered from the iDoE is compared to DoE results. The results suggest that the number of experiments can be reduced by a factor of three to two, meaning less than half of the experiments of a classical DoE are required with the iDoE method. In addition, the understanding of the process dynamics is much improved, which is of particular importance to assess the impact of temporal deviations in the factors on the process response. It also seems possible to integrate the process development activities better with the development of the process control strategy. **Moritz von Stosch,** Senior Manager Fermentation, **GlaxoSmithKline**

	BIOANALYTICAL CONGRESS	CELL CULTURE & UPSTREAM PROCESS DEVELOPMENT	DOWNSTREAM PROCESSING
17:00	**Computational approaches to study biopharmaceutical stability and formulation** As software tools become available for aiding in the design and formulation of biopharmaceuticals, it is necessary to evaluate their usefulness. Such an effort requires collaboration between groups, exchange of data, and ultimately the establishment of benchmark datasets. This presentation will discuss the available predictive tools, their molecular bases, and the scope for providing benchmark evaluations to the wider community of researchers. **Jim Warwicker,** Reader, **Manchester University**	**Biologics manufacturing process improvement using Multivariate Data Analysis: A case study** A legacy biologics manufacturing process exhibited out-of-trend charge isoform levels in the bulk drug substance. Manufacturing data over the last 5 – 7 years were analysed to identify process parameters that influence the charge isoform levels. Multivariate analysis (MVDA) revealed that a few process parameters, namely, viable cell density at feed initiation, feed initiation time, and culture duration, had a strong correlation with the charge isoform levels. An MVDA model comprising these parameters was used to identify optimal ranges of process inputs, which were implemented in manufacturing scale. Several batches of BDS with desired charge isoform profile have since been successfully manufactured. This case study effectively captures the utility of MVDA techniques for understanding and troubleshooting process behaviour. **Anjil Giri,** Development Scientist II, **Alexion Pharamaceuticals**	**In-Line Buffer Conditioning for use in column chromatography processing steps** Large scale manufacture of biologics typically requires large volumes of process solutions. The conventional approach for the supply of these buffers has been to utilise multiple preparation and storage vessels. This tank farm approach requires a large area footprint and high capital investment as well as associated validation, cleaning and maintenance of the buffer preparation and storage equipment. To circumvent this challenge we have introduced an innovative combined In-line Conditioning and Chromatography (ILC-Chrom) system. ILC skids generate buffers in-line from concentrated stocks of acid, base, water and salt allowing formulation of buffers for downstream on-demand. The ILC skid has multiple modes of operation including, recipe/flow feedback, pH feedback and pH & conductivity feedback which can be applied for the generation of buffers. Through a series of pH and conductivity Instruments the ILC can both monitor and control the formulation of buffers to the desired specification. Along with buffer preparation capabilities the ILC-Chrom system allows for integrated chromatography with the prepared buffer delivered directly to the process. The ILC-Chrom system incorporates all the capabilities of a standard production scale chromatography skid. Here, we will outline the pros and cons of the system with respect to the traditional solution preparation approaches in biologics manufacturing. Furthermore, we will discuss the technical aspects of this novel technology and outline some results and learnings generated from Proof of Concept studies and Factory Acceptance Tests of the new equipment. Given the advantages this system provides, ILC technology has the potential to become the new standard to which manufacturing facilities are constructed and how downstream processing is operated **James Murphy,** Technical Specialis**t, MSD,** *Ireland*
17:30	**Using Chemical Denaturants to Improve Predictions of Biopharmaceutical Aggregation during Storage** A key obstacle to predicting aggregation is difficulties in isolating the partially folded states believed to be key intermediates in the aggregation pathways. One approach not yet fully explored is to study the self association behaviour of partially or unfolded states under chemically denaturing conditions when they occur at much larger populations. Typically, these measurements are carried out using static or dynamic light scattering in terms of an osmotic second virial coefficient or a diffusion interaction parameter kD. Here we show how to account for the high concentration of denaturants in the data analysis, which if unaccounted for, could lead to data mis-interpretation. We then correlate light scattering measurements of five monoclonal antibodies at high denaturant concentration with their shelf stability. The results indicate there is a window of denaturant concentration over which the self association behaviour provides an indicator for the aggregation propensity upon storage. **Robin Curtis,** Senior Lecturer, **The University of Manchester**		
18:00	*End of BioProduction 2018*		

	MANUFACTURING STRATEGY & TECHNOLOGY	SMART FACTORIES	MICROBIAL MANUFACTURING
17:00	**Biologics manufacturing process improvement using Multivariate Data Analysis: A case study** A legacy biologics manufacturing process exhibited out-of-trend charge isoform levels in the bulk drug substance. Manufacturing data over the last 5 – 7 years were analysed to identify process parameters that influence the charge isoform levels. Multivariate analysis (MVDA) revealed that a few process parameters, namely, viable cell density at feed initiation, feed initiation time, and culture duration, had a strong correlation with the charge isoform levels. An MVDA model comprising these parameters was used to identify optimal ranges of process inputs, which were implemented in manufacturing scale. Several batches of BDS with desired charge isoform profile have since been successfully manufactured. This case study effectively captures the utility of MVDA techniques for understanding and troubleshooting process behaviour. **Anjil Giri,** Development Scientist II, **Alexion Pharamaceuticals**	**Panel Discussion: Workforce 4.0 –What does the future workforce look like in a smart biomanufacturing facility?** • What are the future workforce requirements for manufacturing 4.0? • What does manufacturing 4.0 need on expert and management levels? • People and digital environment - Identifying the right workforce skill set required for digitalisation and where people are needed in automated field?	**Rational design for further advancement of E. Coli expression systems and production processes** In view of a continuously growing number of hosts used for production of recombinant proteins E. coli is still one of the most frequently used microbial expression systems. The rapidly growing knowledge on E. coli´s cell physiology and new molecular technologies represent the basis for rational and efficient molecular modification. Consequently we see increasing product yields, improved quality and a steadily expanding range of proteins which can economically be produced with E. coli. However, there is still potential for further improvements especially in context with the synchronization/harmonization of host cells capabilities, recombinant protein production and fermentation process design. Our approach in this context aims at a reduction of the recombinant system to the absolute required minimum in order to avoid nonessential burden in expression systems and to follow a "minimal invasive" host cell design approach. We have also established alternative E. coli system that is based on decoupling recombinant protein production and cell growth. The system can be used to produce toxic proteins that would otherwise interfere with cell growth. However, we also observed higher specific protein yields even for proteins that can be efficiently produced with conventional E. coli systems. With respect to production and scale-up the system is fully scalable and high specific protein concentrations also supports down-stream processing. **Gerald Striedner,** Assoc. Prof., **Univ. of Nat. Resources and Life Sciences**
17:30			
18:00	*End of BioProduction 2018*		

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