19-21 March 2019
Sheraton Lisboa Hotel & Spa
Lisbon, Portugal

CHI’s 2ND ANNUAL
BIOPROCESSING
SUMMIT EUROPE
PRACTICAL SOLUTIONS FOR TODAY’S
BIOPROCESS CHALLENGES

CONFERENCE PROGRAMS

STREAM #1
Upstream Processing

STREAM #2
Downstream Processing

STREAM #3
Cell & Gene Therapy

PLENARY KEYNOTE PRESENTERS

Stefanos Grammatikos, PhD
Vice President, Head, Biotech Sciences, UCB Pharma

Markwin Velder, PhD
Vice President, Operations, Managing Director, Kite Pharma EU B.V.

PREMIER SPONSORS

NANO TEMPER
Vironova

CLICK HERE TO REGISTER ONLINE
BioprocessingEurope.com

A Division of Cambridge Innovation Institute
About Bioprocessing Summit Europe

**Bioprocessing Summit Europe** brings together leading upstream, downstream and biomanufacturing scientists to share day-to-day challenges and practical solutions for today's bioprocessing needs. Now in its second year, this six-conference event presents the latest science, case studies, technology updates, and best practices in cell culture, scale-up, recovery, purification, continuous manufacturing, process intensification, and, new for 2019, cell and gene therapy CMC and manufacturing. The Summit also features two Training Seminars, six Short Courses, interactive Breakout Sessions, a joint Plenary Keynote session, and a lively Exhibit Hall to provide in-depth coverage of critical bioprocess topics.

Conference At-A-Glance

### Upstream Processing
- **Stream #1**
  - **19-20 March**: Optimising Cell Culture Technology
- **Stream #2**
  - **19-20 March**: Continuous Processing
  - **20-21 March**: Bioproduction: Scale, Bioreactors & Disposables
- **Stream #3**
  - **19-20 March**: Cell Therapy CMC and Manufacturing
  - **20-21 March**: Gene Therapy CMC and Manufacturing

### Downstream Processing
- **Stream #1**
  - **19-20 March**: Continuous Processing
  - **20-21 March**: Advances in Recovery and Purification

### Cell & Gene Therapy
- **Stream #1**
  - **19-20 March**: Design of Experiments for Bioprocess Analysis
  - **20-21 March**: Intro to Bioprocessing

I particularly liked the mix of industrial and academic speakers covering cutting-edge topics and facilitating stimulating discussions about current practices and future directions of cell culture process development.

Frank Baganz, PhD, Senior Lecturer/Associate Professor, Biochemical Engineering, University College London (UCL)
Short Courses

Monday 18 March, 13:00 – 16:00

SC1: CONTINUOUS PROCESSING MASTERCLASS
The manufacture of biopharmaceuticals using semi- or fully continuous processes has the potential to improve product quality and increase the productivity of biomanufacturing facilities. This short course details the principles and practical challenges of implementing a continuous process strategy. Using examples and shared experiences, the course covers continuous processing definitions and drivers, technologies and processes, process development and control, and quality considerations.
Instructor: Margit Holzer, PhD, Owner, Ulysse Consult

SC2: POTENCY ASSAYS FOR CELL AND GENE THERAPIES
Potency assays are an essential concept in determining the quality of any biological medicinal product/biologic. Extending this concept to cell and gene products is more challenging and often the most difficult aspect of characterising these products. The relevance of the approach taken is often challenged by regulators both during development and when seeking market approval. This workshop will lead you through the issues and how to develop an overall potency strategy.
- What is potency and why is it so important?
- How do I develop potency assays?
- What are the regulatory expectations for potency assays?
Instructor: Christopher Bravery, PhD, Consulting Regulatory Scientist, Consulting on Advanced Biologics, Ltd.

Wednesday 20 March, 18:30 – 21:00

SC5: SAVING TIME IN PROCESS DEVELOPMENT WITH NEXT-GENERATION METHODS: iDoE, HYBRID MODELING AND PAT
In this short course, we show how a more accurate design space can be defined that provides increased flexibility for process operation based on the iDoE-hybrid modeling strategy. We also show how advanced monitoring strategies support the tracking of the deviations and how these methods can readily be developed from the iDoE data. It will be illustrated how the combination of the hybrid model with monitoring can directly be exploited for process control, thus naturally evolving the last step of the QbD roadmap.
Instructors: Moritz von Stosch, PhD, Senior Manager, Drug Substance, Technical R&D, GSK Vaccines
Gerald Striedner, PhD, Associate Professor, Biotechnology, University of Natural Resources and Life Sciences (BOKU)
Mark Dürkop, PhD, Project Leader, Biotechnology, University of Natural Resources and Life Sciences (BOKU)

Short Courses

Attending 2018’s Bioprocessing Summit Europe was a really positive experience. The scientific program was excellent and informative, and it was easy to meet people to interact and make new contacts. I would highly recommend attending.

Jonathan Bones, PhD, Principal Investigator, Characterization and Comparability Laboratory, National Institute for Bioprocessing Research and Training (NIBRT)
PLENARY KEYNOTES: NEXT-GENERATION PROCESSES AND PRODUCTS

Chairperson
Manuel Carrondo, PhD, Professor of Chemical and Biochemical Engineering, FCT-UNL, Vice President, IBET

Bioprocessing Innovations in the Era of Clinical Acceleration and Process Intensification
Stefanos Grammatikos, PhD, Vice President, Head, Biotech Sciences, UCB Pharma

Stefanos Grammatikos is heading Biotech Sciences, the biologics CMC development organization of UCB. He is overseeing drug substance/API, formulation, drug product, analytical methods and primary and secondary packaging development for all of UCB’s pipeline biologics from candidate selection to market launch. Stefanos joined UCB in 2008 attracted by the opportunity to build new biotech capacities, capabilities and expertise and thus help the company realize its aspiration to bring to patients innovative biotech products and become a leader in biopharmaceuticals. Under his direction highly expert teams and a number of state-of-the-art facilities were built and high performance platforms for UCB’s mammalian cell culture and microbial products have been realized.

Opportunities and Challenges in CAR T Manufacturing
Markwin Velders, PhD, Vice President, Operations, Managing Director, Kite Pharma EU B.V.

Dr. Markwin Velders brings over 18 years of management experience in biotechnology companies. He obtained his PhD from Leiden University and after a post-doc and associate professorship at Loyola University in Chicago, he became Chief Scientific Officer at AM-Pharma. After bringing two compounds from bench to bed at AM-Pharma, Markwin moved to TNO Biosciences as a Business Unit Manager, managing a group of 150 professionals. Since 2011 he has been independently active as Prime Life Science, assisting various start-up and early life science companies with their strategy, financing, business development and interim management. He has been involved in the start-up of several new ventures, and secured funding for 4 Life Science start-ups.

Upstream Processing

Downstream Processing

Cell & Gene Therapy
Monday, 18 March

13:00 - 16:00 Recommended Short Course*
SC3: Optimising Cell Culture Media
*Separate registration required, see page 5 for details.

Tuesday, 19 March

7:00 Registration and Morning Coffee

MODELING & NEXT-GEN METHODS

8:25 Chairperson’s Opening Remarks
Kerstin Otte, PhD, Professor, Institute of Applied Biotechnology (IAB), Pharmaceutical Biotechnology (PBT), Birkbeck University of Applied Sciences

8:30 Should the Dynamic Nature of Process Operation Be Reflected by the Design Space Representation/Characterization?
Moritz von Stosch, PhD, Senior Manager, Drug Substance, Technical R&D, GSK Vaccines
The majority of design spaces described in publications follows a “static” statistical experimentation and modeling approach. Given that temporal deviations in the process parameters are of a dynamic nature, static approaches do not suffice. I will discuss alternative forms of design space representations and illustrate the limitations of the predominantly applied static approach. These approaches may create an opportunity to integrate process characterization, process monitoring and process control strategy development as defined in the Quality by Design workflow.

9:00 Towards Model Predictive Control of Cell Culture Bioprocesses
Gerald Striedner, PhD, Associate Professor, Biotechnology, University of Natural Resources and Life Sciences, Vienna (BOKU)
Today, quality by testing is still the gold standard in bioprocesses. The production process is fixed and tightly specified to guarantee a constant product quality. However, out-of-specification events often result in batch rejections. Therefore, we applied intensified Design of Experiment (DoE) to quickly screen a defined design space of a CHO fed-batch process. Hereby, a hybrid model is created that is enhanced by the data. This model will be used in the future for model predictive control to avoid batch rejections.

9:30 Digital Twins for Process Robustness and Control Strategies
Christoph Herwig, PhD, Professor and Head, Biochemical Engineering, Chemical Environmental and Bioscience Engineering, Technical University of Vienna (TU Wien)
Digital twins get increased attention due to novel enablers of digitalization, but also due to regulatory encouragements such as ICH Q12. But how to use them for fulfilling industrial needs, such as achieving higher process robustness and smooth accelerated process validation? The contribution introduces concepts and case studies in which digital twins are deployed for smart experimental design and model-based control.

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

10:45 Modeling and Optimising Fed-Batch Cell Culture Dynamics
Sakhr Alhuthali, PhD Student, Chemical Engineering, Imperial College London
We used a mathematical model to optimise the feeding strategies and temperature shift point to improve the product titre. We managed to extend the cell culture duration to increase productivity and reduce the accumulation of process-related impurities, HCP. This model can be used to understand the process dynamics in scale-up and to implement the optimum control strategies.

A nice and friendly meeting fostering relaxed, easy going but efficient interactions with participants and companies.

Florian M. Wurm, PhD, Professor Emeritus, Swiss Federal Institute of Technology Lausanne (EPFL), and Founder & CSO, ExcellGene SA

11:15 Intensified Design of Experiments – An Approach to Reduce Bioprocess Development and Characterization Times
Mark Dürkop, PhD, Project Leader, Biotechnology, University of Natural Resources and Life Sciences, Vienna (BOKU)
One of the bottlenecks in the development of innovative biopharmaceuticals is found in endless process development and characterization times. Within this work, we compared classical Design of Experiments (DoE) with an intensified DoE approach applied on an E. coli fed-batch process. While the screening of a classical DoE required 29 weeks, the intensified characterization was finished within 10 weeks unveiling both the best process conditions and dynamics. The generated model can further be applied for process control.

11:45 Next Generation Single-Cell Dispensing in Cell Line Development
Thomas Kretzschmann, Field Application Specialist, cytenta
Cytenta’s single-cell deposition technology isolates single, living cells automatically in 96- and 384-well plates in a documented, viable and pure workflow. The single-cell printer and the new x.sight instruments provide assurance of clonality, high cell viability, no cross-contamination by the use of disposables and are easy to use.

12:00 Continuous In-Line Cell Counting and Infection Kinetics Monitoring, a Case Study
Sean Case, Scientist, Process Cell Culture: Upstream Scale Up Group, Novavax
Inline, label-free and in real time viral infection kinetics with fed batch process including two different recombinant protein targets; comparability at 10 L
13:35 Keynote Presentation: Proteomic and Phosphoproteomic Characterisation of Growth of Recombinant Chinese Hamster Ovary Cells
Paula Meleady, PhD, Associate Director, National Institute for Cellular Biotechnology, Dublin City University

Phosphorylation is a hugely important post-translational modification, playing a crucial role in regulating many cellular processes. We describe the proteomic and phosphoproteomic characterization of CHO cells during growth in culture and in cells subject to temperature shift. Using advanced LC-MS/MS techniques, we have characterised >8000 CHO-specific phosphorylation sites and identified >1500 differentially expressed phosphopeptides in these studies. Phosphoproteins have the potential to be cell engineering targets to improve efficiency of recombinant protein production.

14:05 Engineering CHO Cell Lines for the Production of Hard-to-Produce Proteins
Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark (TU Denmark)

Using our high-throughput cell line engineering platform, we have engineered CHO cells that are able to produce therapeutic proteins that previously were not possible to produce in CHO cells. This approach may result in improved therapeutic proteins with better biological properties such as increased half-life, improved activity, etc.

14:35 Difficult to Express Proteins: Identification of Intracellular Production Bottlenecks in CHO Cells
Kerstin Otte, PhD, Professor, Institute of Applied Biotechnology (IAB), Pharmaceutical Biotechnology (PBT), Biberach University of Applied Sciences

With the advance of complex biological format proteins, mammalian expression systems often show low performance. Determining factors may be haltering of heterologous proteins within the different cellular compartments disturbing transport or secretion. Here we present a streamlined microscopy-based methodology for CHO production cells investigating rate-limiting steps in production organelles, which is also applicable for automated applications in industrial cell line development processes. Characterisation of identified haltering cellular structures will enable engineering approaches for optimized cellular production.

15:05 Refreshment Break in the Exhibit Hall with Poster Viewing

Paul Kelly, PhD, Postdoctoral Research Scientist, Cell Engineering Lab, National Institute for Bioprocessing Research and Training (NIBRT)

Chinese hamster ovary (CHO) cells remain the dominant production host for recombinant therapeutic proteins within the biopharmaceutical industry. Further enhancing their ability to manufacture these complex therapies in large quantities as well as shortening cell line development timelines has been the focus of CHO cell biologists over the past 3 decades. Genetic engineering strategies using microRNAs (miRNAs) to augment CHO cell bioprocessing performance have proved promising but require a greater deal of understanding.

16:15 In silico Culture Media Design Based on Prior Metabolic Knowledge
Rui Oliveira, PhD, Associate Professor, Systems Biology and Engineering (SBE), Chemical Engineering & Biochemistry, Universidade Nova de Lisboa

In this talk, a rational methodology to design culture media composition based on biochemical networks is presented. The method consists of a systems approach to generate hypothesis on the concentrations of organic compounds, mineral macro- and microelements in culture media using a priori knowledge on the metabolic network of the target cells. Although not completely eliminating the need for experimental testing, this rational approach significantly reduces the experimental burden in comparison to statistical DoE-based methodologies.

16:45 Breakout Discussion Groups
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. Then continue the discussion as you head into the lively exhibit hall for information about the latest technologies.

17:30 Welcome Reception in the Exhibit Hall with Poster Viewing

Wednesday, 20 March

8:00 Registration and Morning Coffee

Monitoring Quality & Enhancing Productivity

8:25 Chairperson’s Remarks
Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark (TU Denmark)
8:30 Monitoring the Metabolic State and Productive Capacity of Cells during a Bioprocess
Michael Butler, PhD, CSO, Research, National Institute of Bioprocessing Research & Training (NIBRT)
Maintenance of cell viability during a bioprocess is crucial for productivity and product quality. The traditional approach involves off-line testing using dye exclusion at fixed points throughout the process. Novel methods of on-line digital holography, dielectric spectroscopy and impedance flow cytometry can provide a more complete picture of the state of cells during a bioprocess. Such methods compare well with off-line dye exclusion methods and conventional flow cytometry.

9:00 Increasing HEK293-Based Bioprocess Productivity by Means of Both Specific Productivity Improvement and Cell Culture Strategic Development
Martí Lecina Veciana, PhD, Associate Professor, Bioengineering, Institut Químic de Sarrià, Universitat Ramon Llull (URL)
The enhancement of the economical sustainability of bioprocesses requires an increase of the volumetric productivity, which can be improved by means of genetic engineering (higher specific cell productivity) and/or by bioprocess engineering (increasing cell density). For the latter, reliable online measuring systems for cell density and metabolic activity estimation have been developed as a tool for nutrient feeding estimation in fed-batch cultures. A compilation of different pieces of work covering all these aspects related to bioprocess optimization will be discussed.

9:30 Process Intensification
David Brühlmann, PhD, Manager, Biotech Process Sciences Technology & Innovation, Merck Healthcare Process intensification in upstream bioprocesses to enhance cell culture productivity has become more frequent. This presentation provides insight into the development of an intensified fed-batch platform process, which enables increased process efficiency with a smaller footprint. Examples include the production of various monoclonal antibodies and a fusion antibody, showing 2-4x titer increases with comparable product quality to classical fed-batch processes.

10:00 Sponsored Presentation (Opportunity Available)

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

Plenary Session: NEXT-GENERATION PROCESSES AND PRODUCTS

11:15 Chairperson’s Remarks
Manuel Carrondo, PhD, Professor of Chemical and Biochemical Engineering, FCT-UNL; Vice President, IBET

Stefanos Grammatikos, PhD, Vice President, Head, Biotech Sciences, UCB Pharma
Current trends in clinical development acceleration and bioprocess intensification impose an unprecedented compression of CMC development timelines and new bioprocessing challenges downstream of the cell culture bioreactor. In this talk I will present a series of innovations we have introduced, some incremental and some potentially disruptive, in an effort to avoid further complications while rising to the latest challenges of bio CMC development and bioprocessing.

11:50 Opportunities and Challenges in CAR T Manufacturing
Markwin Velders, PhD, Vice President, Operations, Managing Director, Kite Pharma EU B.V.
Update on the status of CAR-T development for use in the treatment of cancer. The success story of this paradigm shift and the challenges and opportunities that lay ahead for this therapy will be presented and discussed.

12:20 Close of Conference

12:30 Bridging Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own
Wednesday, 20 March

10:00 Registration Open
10:30 Coffee Break in the Exhibit Hall. Last Chance for Poster Viewing.

Plenary Session: NEXT-GENERATION PROCESSES AND PRODUCTS
11:15 Chairperson's Remarks
Manuel Carrondo, PhD, Professor of Chemical and Biochemical Engineering, FCT-UNL, Vice President, IBET

Stefanos Grammatikos, PhD, Vice President, Head, Biotech Sciences, UCB Pharma

Current trends in clinical development acceleration and bioprocess intensification impose an unprecedented compression of CMC development timelines and new bioprocessing challenges downstream of the cell culture bioreactor. In this talk I will present a series of innovations we have introduced, some incremental and some potentially disruptive, in an effort to avoid further complications while rising to the latest challenges of bio CMC development and bioprocessing.

12:20 Session Break
12:30 Bridging Luncheon Presentation
Sponsored by
FUJIFILM

13:00 Session Break

HARNESSING DATA AND MODELING TO IMPROVE BIOPROCESSES
13:40 Chairperson's Opening Remarks
Ronan O'Kennedy, PhD, Consulting Bioprocess Specialist, ROK Bioconsulting

13:45 KEYNOTE PRESENTATION: Big Data and Bioengineering: The Perfect Marriage
Arlindo Oliveira, PhD, Professor, Computer Science & Engineering, Instituto Superior Técnico

Modern artificial intelligence techniques, heavily based on machine learning approaches, have created the possibility to analyze large volumes of data in many domains in ways that were inaccessible until now. Modern bioengineering depends heavily, if not totally, on data-based approaches that are able to uncover the knowledge hidden in the large amounts of data generated by genomics, proteomics, metabolomics and other "omics". This talk will describe some methodologies that can be used to extract knowledge from biological data and to direct bioengineering research.

14:15 Mathematical Modelling Across Reactor Scales
Krist Gernaey, PhD, Professor, Head, Process and Systems Engineering Center (PROSYS), Chemical and Biochemical Engineering, Technical University of Denmark

Modelling plays an increasingly important role in bioprocess development. Computational Fluid Dynamics (CFD) is now generally used as a tool for the description of bioreactor hydrodynamics, also at large scale. CFD will be presented as a modelling framework forming the basis for development of compartment and scale-down models. Furthermore, challenges related to model validation and potential solutions are highlighted, and future perspectives related to advanced modelling frameworks are presented.

14:45 Individual-Based Models for Bioprocesses
Rebeca González-Cabaleiro, PhD, Lecturer, Infrastructure & Environment, Engineering, University of Glasgow
Microbial communities are complex. Our lack of knowledge makes our capacity to engineer them limited and biosystems are in many cases unpredictable. This reduces the interest of bio-based industrial processes and therefore the full versatility and potential of these systems remain unexploited. Mathematical models at the micro-scale level are a perfect tool to describe the heterogeneity of microbial communities, explore their capacities and predict their behavior.

15:15 Presentation to be Announced
Sponsored by

15:30 A Software Platform for Quality by Control Realization of Bioprocesses
Wolfgang Sommeregger, PhD, Research & Development, Bilfinger Industrietechnik Salzburg GmbH

We present an advanced process monitoring and control software, capable of data-integration, -processing and -management, modeling and control, ultimately enabling PAT integration to bioprocesses. The data for the establishment of the software was generated by applying a design of experiments setting to recombinant CHO bioprocesses at different scales.

15:45 Refreshment Break in the Exhibit Hall with Poster Viewing
### MONITORING QUALITY

**16:25 Online Monitoring in Microfluidics and Micro(bio)reactors with Integrated Optical Chemical Sensor**

Torsten Mayr, PhD, Associate Professor, Analytical Chemistry, Graz University of Technology (TU Graz)

We present the miniaturization and integration of optical chemical sensors for oxygen, pH and glucose in microfluidic and micro-bioreactors. Miniaturized sensor layers and spots in sizes down to 100 micrometers are read out with miniaturized instruments. In addition, luminescent nanobeads are demonstrated as an attractive alternative to integrated sensor layers since they can be easily injected into the flow, do not interfere with the sample, and have fast response times.

**16:55 High Resolution Native LC-MS for Product CQA Assessment and Process Monitoring**

Jonathan Bones, PhD, Principal Investigator, Characterization and Comparability Laboratory, National Institute for Bioprocessing Research and Training (NIBRT)

Multi-attribute monitoring has attracted considerable attention recently as process scientists request more information to assist them to develop and understand their bioprocesses. A strategy for multi-attribute monitoring using intact protein separations coupled to native high resolution mass spectrometry will be described that facilitates the determination of multiple product quality attributes such as glycosylation, deamidation, lysine truncation, etc. Different examples will be presented along with strategies for inclusion of the platform in an online format.

**17:25 Risk Management in ICH Q12: Supporting Quality, Compliance & Culture Excellence Over Lifecycle of Biologic Products**

José Monteiro Cardoso de Menezes, PhD, Associate Professor, Pharmaceutical Engineering, Institute for Biotechnology & Bioengineering, Institute Superior Técnico, University of Lisboa, and CEO, 4Tune Engineering

RM is to KM what PAT is to QbD! Although presently the industry may lack better ways to manage knowledge (KM) through sophisticated tools and platforms, risk-management (RM) tools can provide very effective capabilities to capture, retain, and support knowledge-driven lifecycle activities. There is a recent regulatory expectation (ICH Q12) that companies can retrospectively use key QbD elements (e.g., RM) to address and justify improvements in their current legacy control strategies, supporting post-approval changes using risk- and knowledge-based approaches.

### NEXT-GENERATION STRATEGIES

**8:25 Chairperson’s Opening Remarks**

Jonathan Bones, PhD, Principal Investigator, Characterization and Comparability Laboratory, National Institute for Bioprocessing Research and Training (NIBRT)

**8:30 FEATURED PRESENTATION: Next-Generation Processes, Technologies and Operations**

Michael Pohlscheidt, PhD, Site Head & Head of Operations, Solothurn Manufacturing Facility, Biogen

A critical step in meeting the demand of biologic production worldwide involves implementing disruptive manufacturing technologies, processes and capabilities. This talk will evaluate Biogen’s new manufacturing site in Switzerland, due to go online in 2019, including the new processes, operational models and technologies being adopted to drive value through innovation and deliver new medicines in areas such as Alzheimer’s.

**9:00 Characterisation and Application of a Miniature Bioreactor System for Cell Culture Process Development**

Frank Baganz, PhD, Associate Professor, Biochemical Engineering, University College London (UCL)

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

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

Michael Pohlscheidt, PhD, Site Head & Head of Operations, Solothurn Manufacturing Facility, Biogen
10:00 Improving the Yields of Complex Monoclonal Antibodies and Fusion Proteins for Cancer Therapy
Peter Blas, PhD, Lecturer, Biochemical Engineering, University College London (UCL)
The bioprocessing of a fusion protein is characterised by low yields, and through recovery and purification, an overall 90% loss. However, there is evidence of the protection of degradation products which occurs in the presence of shear plus air/liquid interfaces. This study seeks to characterise the loss and use of ultra-scale-down studies to predict its occurrence; and shows loss may be diminished by the use of protective reagents, such as Pluronic F68.

10:30 Coffee Break in the Exhibit Hall. Last chance for poster viewing.

SINGLE-USE SYSTEMS
11:15 Scaling Up and Down of Single-Use Bioreactor Cultivations
Stefan Junne, PhD, Group Leader & Chair, Bioprocess Engineering, Technische Universität Berlin
Process scalability has been an issue for over 50 years in the area of stainless steel bioreactors. Methods for the characterization of industrial-scale bioreactors and scale-down systems have been established; however, this subject gained new relevance by the various designs of single-use bioreactors. Therefore, the current state of scaling up and down single-use bioprocesses are presented and discussed based on examples from typical cell culture to niche applications, which offer new possibilities for single-use based bioprocessing.

11:45 A DOE Approach to Oxygen Transfer Modelling in Single-Use Bioreactors
Ronan O’Kennedy, PhD, Consulting Bioprocess Specialist, ROK Bioconsulting
A DOE approach was used to characterize the effects of total gas flow-rate, % inlet O₂, conc, agitation, and % fill volume on KLa in three single use bioreactor scales commonly used for process development and scale up. The relative effects of operating parameters and interactions at each scale were evaluated. We show that the combined model can be used to make accurate predictions of KLa across the 2 – 200 L bioreactor range, thereby simplifying the scale up of the upstream processes.

12:15 De-Intensifying Protein Production with Pichia pastoris
Diether Mattanovich, PhD, Professor, Microbial Strain Design, Biotechnology, University of Natural Resources and Life Sciences (BOKU)
The yeast Pichia pastoris is well established for production of heterologous proteins for technical and biopharmaceutical use. The major benefit, i.e., high expression levels on methanol, driven by methanol inducible promoters, is also the source of a major drawback: methanol utilization leads to high oxygen consumption and metabolic off-flavor. Here, we present a strategy to produce proteins with novel methanol independent promoters which enables a simple and fast process regime, exceeding methanol processes in titer and productivity. This strategy can save installation and operation costs, and make P. pastoris amenable for single-use bioreactors.

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

13:15 Session Break

PROCESS IMPROVEMENTS
13:45 Chairperson’s Remarks
Stefan Junne, PhD, Group Leader & Chair, Bioprocess Engineering, Technische Universität Berlin

13:50 Bioprocessing of Cell Culture Derived Vaccines
Leeann Naicker, PhD, Researcher, Research and Development, OBP Vaccines
Currently, we are evaluating various Bioreactors for the production of vaccines. These processes will be adopted into our GMP facility. Various parameters are being assessed, including pH, glucose consumption, online monitoring, dissolved oxygen, cell production, virus production, scaling up, and effects of shear stress. Bioreactors such as the Tide cell, Bello cell, Icellis, Biostat stirrer tanks have been evaluated, and currently the Biostat Cultibag is being evaluated for cell and vaccine production.

14:50 Characterization of Mammalian Cell Culture Off-Gas Composition by On-Line Magnetic Sector MS for Real-Time Bioprocess Monitoring
Patrick Floris, PhD, Researcher, National Institute for Bioprocessing Research and Training (NIBRT)
The evaluation of a magnetic sector MS analyser, the Prima BT from Thermo Fisher Scientific, as an on-line technology for mammalian cell culture process monitoring is here presented. Through off-gas monitoring, dissolved oxygen, cell production, virus production, scaling up, and effects of shear stress, bioreactors such as the Tide cell, Bello cell, Icellis, Biostat stirrer tanks have been evaluated, and currently the Biostat Cultibag is being evaluated for cell and vaccine production.

15:20 Close of Conference
Continuous Processing
Increasing Process Intensification and Control

Monday, 18 March

13:00 - 16:00 Recommended Short Course*
SC1: Continuous Processing Masterclass
*Separate registration required, see page 5 for details.

Tuesday, 19 March

7:00 Registration and Morning Coffee
FROM PERFUSION TO PURIFICATION

8:25 Chairperson’s Opening Remarks
Alois Jungbauer, PhD, Professor, Department of Biotechnology, University of Natural Resources and Life Science, Vienna, Austria and Austrian Centre of Industrial Biotechnology

8:30 FEATURED PRESENTATION: Continuous Manufacturing: Transitioning from Batch to Continuous Economics Implications
Andrew Sinclair, President & Founder, Biopharm Concepts Ltd.
In the transition from batch to continuous processing, it is important to assess the impact of continuous operation in downstream processing and to determine the optimal level of continuous technology integration. In this analysis, bioprocess modelling is used to assess the level of continuous technology that makes economic sense. The basis of the process model is that standard monoclonal antibody process defined by Biophorum’s technology roadmap team. This is used as a reference measure the impact of innovative technologies.

9:00 Development of Perfusion Scale-Down Models for Medium Development
Amy Johnson, PhD, Associate Director, Cell Culture and Media Development, Regeneron
Due to the complex nature of bioreactor medium, high throughput 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.

9:30 More than 15 Years of Continuous Processing Using Chemostat Cultures – Turning Concepts into Reality
Daniel Fleischanderl, Manager, Process Development, Shire
The talk summarizes Shire’s almost unique approach using continuous chemostat cultures for routine commercial production of blood clotting factors. It describes the process, the technology and obstacles applying this approach. The main part will elaborate on scaling up beyond 10k and transfer to single use.

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

10:45 Process Modelling of CHO Cell Perfusion Continuous Culture
Srinivas Suda, PhD, SFI Industry Research Fellow, NIBRT
Continuous perfusion culture with high cell densities require a high level of process understanding, real-time monitoring and multivariate data analysis to predict suitable process conditions. In situ Raman spectroscopy enables real-time monitoring for multivariate parameters and can be used for in-line control to maintain process conditions through metabolite manipulation. CHO DP12 cells grown in continuous perfusion culture with process modelling and automatic feedback control in real time to control process conditions will be discussed.

11:15 KEYNOTE PRESENTATION: Breaking Barriers to Manufacturing: Innovation with Continuous Flow Technology
Marcus Faddeiro, PhD, Associate Director, DSP Continuous Manufacturing, Sanofi

11:45 Co-Presentation: To Switch from Chromatography Skid to DSP Skid: What For?
Thomas Flouquet, Application Specialist, Equipment Process Solutions, Novasep
Abir Banerjee, Deputy General Manager, Ensene Biosciences Ltd
Today most of the biopharma companies are looking to implement continuous intensified processes in order to reduce the costs of drugs production. Thomas Flouquet will present how to develop the smartest process ever by combining multi-column and batch chromatography on a single DSP unit and the main associated benefits (productivity boost, COGs and footprint reduction and better product quality). Be ready for a revolution!

12:15 Luncheon Presentation (Sponsorship Opportunity Available)

12:45 Session Break

PROCESS INTEGRATION AND INTENSIFICATION

13:30 Chairperson’s Remarks
Margit Holzer, PhD, Scientific Director, Ulysse-Consult

Michael Rose, Senior Scientist, Downstream Processing Department, UCB
As biopharma struggles under tightening budgets, competition and complex molecule formats, efforts are underway to intensify manufacturing. Periodic Counter Current (PCC) and Multi-Column Solvent Gradient Purification (MCSGP) are continuous systems that improve capacity, buffer use, productivity, yield and purity. We take a deep look at hidden pitfalls in these emerging multi-column technologies and suggest mitigation strategies. We also introduce two new techniques that adapt MCC concepts on traditional column systems and maximise performance while minimising complexity.
14:05 An Integrated Multistep Purification Approach Including Online Monitoring
Florian Disner, PhD, Downstream Technologies, Global Research Technologies, Novo Nordisk
The presentation targets reduction of lead times for both process development and variant production by combining a fully automated, closed modification and purification platform with online and very fast at-line analytics. The combination of both technologies could potentially result in a generic, scalable setup that can be used independent of the molecular format of interest and does not require affinity purification steps. Here a case study is presented to show an end-to-end purification platform combined with the analytical power of a diode-array detector for the production of an enzymatically modified peptide variant.

14:35 Real Continuous Downstream Processing without Cycling Operation
Alois Jungbauer, PhD, Professor, Department of Biotechnology, University of Natural Resources and Life Science, Vienna, Austria and Austrian Centre of Industrial Biotechnology
In continuous downstream processing a cyclic or a quasi-continuous operation is required when the product is adsorbed on a chromatography sorbent. A process for purification of antibodies is shown which is truly continuous with non-interrupted flow of the product stream. This allows the implementation into a fully continuous integrated process.

15:05 Refreshment Break in the Exhibit Hall with Poster Viewing

15:45 Continuous Virus Inactivation Process Using a Novel Packed-Bed Reactor
Duarte L. Martins, PhD Student, BOKU/ACIB, Laboratory of Protein Technology and Downstream Processing, Department of Biotechnology, University of Natural Resources and Life Sciences (BOKU)
Continuous virus inactivation has been overlooked while the biopharma industry moves towards continuous integrated processing. A novel continuous virus inactivation setup, which has several advantages over other approaches, will be presented. Solvent/detergent treatment was successfully employed for the continuous virus inactivation of two-industry standard virus models (X-MuLV and BVDV). Control experiments are presented showing that the continuous setup is as effective as the batch incubation.

16:15 Advances in Continuous Manufacturing
Matteo Costioli, PhD, Director, Head of NBEs, Early Process Development, Merck Serono

16:45 Breakout Discussion Groups
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. Then continue the discussion as you head into the lively exhibit hall for information about the latest technologies.

17:30 Welcome Reception in the Exhibit Hall with Poster Viewing
9:30 Towards Industry 4.0 - Process Data Management and Analysis for Automated and Digitalized Bioprocessing
Michael Sokolov, PhD, Postdoctoral Fellow and Lecturer, Institute of Chemical and Bioengineering, ETH Zurich
Several important trends have been observed in bioprocessing towards more robust and automated operations. Continuous bioprocessing and data acquisition as well as the utilization of data- and knowledge-driven tools for process analysis and control thrive towards the standards of industry 4.0. Based on industrial case studies this presentation will highlight the enabling role of advanced process modeling for bioprocess digitalization and automation.

10:00 Why, How, When Outsourcing Buffers: Footprint Challenges in Downstream Processing
Rémy Collier, Product Manager, Downstream Buffers & Delivery Systems, Cell Culture Media, Sartorius Stedim FMT S.A.S
Preparing buffers is a not a value adding activity in the manufacture of biologics but requires considerable resources. Buffer preparation takes investment in time and can be challenging to achieve the target specification. Performing the necessary quality tests incurs further costs. Management of the supply chain for the myriad of individual components is also time consuming.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:15 Chairperson's Remarks
Manuel Carrondo, PhD, Professor of Chemical and Biochemical Engineering, FCT-UNL; Vice President, IBET

Stefanos Grammatikos, PhD, Vice President, Head, Biotech Sciences, UCB Pharma
Current trends in clinical development acceleration and bioprocess intensification impose an unprecedented compression of CMC development timelines and new bioprocessing challenges downstream of the cell culture bioreactor. In this talk I will present a series of innovations we have introduced, some incremental and some potentially disruptive, in an effort to avoid further complications while rising to the latest challenges of bio CMC development and bioprocessing.

11:50 Opportunities and Challenges in CAR T Manufacturing
Markwin Velders, PhD, Vice President, Operations, Managing Director, Kite Pharma EU B.V.
Update on the status of CAR-T development for use in the treatment of cancer. The success story of this paradigm shift and the challenges and opportunities that lay ahead for this therapy will be presented and discussed.

12:20 End of Conference

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

NEXT-GENERATION PROCESSES AND PRODUCTS

11:15 Chairperson’s Remarks
Manuel Carrondo, PhD, Professor of Chemical and Biochemical Engineering, FCT-UNL, Vice President, IBET

Stefanos Grammatikos, PhD, Vice President, Head, Biotech Sciences, UCB Pharma

Current trends in clinical development acceleration and bioprocess intensification impose an unprecedented compression of CMC development timelines and new bioprocessing challenges downstream of the cell culture bioreactor. In this talk I will present a series of innovations we have introduced, some incremental and some potentially disruptive, in an effort to avoid further complications while rising to the latest challenges of bio CMC development and bioprocessing.

11:50 Opportunities and Challenges in CAR T Manufacturing
Markwin Velders, PhD, Vice President, Operations, Managing Director, Kite Pharma EU B.V.

Update on the status of CAR-T development for use in the treatment of cancer. The success story of this paradigm shift and the challenges and opportunities that lay ahead for this therapy will be presented and discussed.

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

13:00 Session Break

OPTIMIZING DSP

13:40 Chairperson’s Opening Remarks
David O’Connell, PhD, Lecturer in Biotherapeutics, School of Biomolecular & Biomedical Science, University College Dublin


14:15 Validation of Next-Generation Depth Filter Technology in a Commercial Downstream Process
Kim Hermans, PhD, Team Lead, MSAT Purification, Sanofi

14:45 Centrifugation Scale-Up Modelling
Daniel Kronberger, PhD, Head, Downstream Pilot, Process Science, Boehringer Ingelheim

In bioprocess development centrifugation steps continue to be a major element of uncertainty during scale up. Varying centrifugation performance causes differences in product recovery and purity and may interfere with subsequent unit operations such as depth filtration or inclusion body solubilization. The main cause for performance variance lies in the different types of centrifuges and separators that are in use at different scales. Current scale up strategies are only effective if both devices are functionally identical. However, most construction types are either principally not suitable or not obtainable for all scales.

15:15 Raman Monitoring of Downstream Bioprocesses: Opportunities to Fix Analytical Bottlenecks
Christophe Bonneville, President, RESOLUTION Spectra Systems

In-line Raman spectroscopy demonstrates strong capabilities to monitor key parameters, such as structure and conformation of proteins, titer, purity, enabling to monitor some downstream processes. From a QC perspective, this technique is also efficient to quickly control product CQA. However, in order to widely implement this technology, some issues need to be carefully taken care of: validity, robustness and transferability of models over time, process evolution and devices. We will present opportunities based on examples.

15:45 Refreshment Break in the Exhibit Hall with Poster Viewing

16:25 Removal of High-Molecular-Weight Species by Protein A Chromatography
Danielle van Wijk, PhD, Lead Scientist, Downstream Processing, Syntho Biopharmaceuticals

In this study, the potential of Protein A chromatography to separate antibody monomer from HMW species was investigated. A design-of-experiments approach was used and shows that HMW species can potentially be separated from antibody monomer by Protein A chromatography to the desired levels while maintaining an acceptable monomer recovery. This would result in the use of a more efficient Protein A step and allow for reduction of DSP economics.

16:55 Affinity Chromatography for the Next Generation of Biotherapeutics, Empirical Approaches to Engineering a Universal Process
David O’Connell, PhD, Lecturer in Biotherapeutics, School of Biomolecular & Biomedical Science, University College Dublin

Developing novel affinity methods for the separation of biomolecules requires the integration of biochemical and biophysical parameters that ensure the protein is delivered in an active, native conformation that will greatly depend on how it is captured and how it is released. This talk will focus on engineering protein
sequences that facilitate specificity and stability without compromising the integrity of the protein product with some recent examples of successful biotherapeutic candidates.

17:25 Modeling and Simulation of Ion-Exchange in Bio-Processes – Illustrations from Industrial Biotech to Biopharma
Roger-Marc Nicoud, CEO, Ypso-Facto
In industrial biotech (citric acid separation, amino-acids purification), complexity of ion exchange phenomena has been modeled and fairly predicted. However, as molecules in biopharma represent a higher degree of complexity, they challenge the rigorous description of ion exchange phenomena involved in their isolation. We will show how to deal with complexity of molecules and ion exchange to bring on hand modeling and consequently a rigorous and competitive design of industrial biopharma processes.

17:55 End of Day
18:00 Dinner Short Course Registration
See page 5 for details.

NEW DSP TECHNOLOGIES AND MODALITIES

8:25 Chairperson's Opening Remarks
David O'Connell, PhD, Lecturer in Biotherapeutics, School of Biomolecular & Biomedical Science, University College Dublin

8:30 KEYNOTE PRESENTATION:
Developing and Processing of Low-Cost Magnetic Particles for Protein Separation in the Technical Scale
Sonja Berensmeier, PhD, Professor, Bioseparation Engineering Group, Department of Mechanical Engineering, Technical University of Munich
We were able to create new peptide tags that bind an inexpensive non-functionalized, bare surface. As adsorber material, we used biocompatible magnetic nanoparticles, a promising material that has shown applicability in a wide range of areas. This work paves the way for a new, economical purification process of biotechnologically produced proteins and contributes to a deeper understanding of bio-nano interactions.

9:00 Generic Buffer System: A Smart Tool for Efficient Next-Generation Downstream Processes
Anja Trapp, Scientist, Bioprocessing Technology & Innovation, Rentschler-Biopharma
New strategies improving protein purification are an inevitable prerequisite for next-generation processes. Our generic buffer system enables a smart development of a simple and economic production process. On this basis, a modular toolbox of separation techniques is used to achieve the desired product quality and purity. The talk will give insights into our flexible approach in form of different case studies.

9:30 A Novel Alkaline Stable Protein
A Resin Based on Monodisperse Agarose Beads
Hans J. Johansson, Global Applications Director – Agarose, Purolite Life Sciences
In contrast to batch emulsification, by utilising a scalable continuous emulsification technology termed ‘jetting’ - beads with a very narrow particle distribution have been manufactured, omitting the need for sieving, and resulting in almost quantitative yield. The performance data of a new range of chromatography resins will be presented.

9:45 Sponsored Presentation (opportunity available)
10:00 Multi-Component Adsorption as a Challenge for Process Chromatography
Rainer Hahn, PhD, Associate Professor, Department of Biotechnology, BOKU
Chromatography is the most effective method when it comes to preparative protein separation, as it provides the highest selectivity and resolution power. However, with complex feed stocks many adsorption systems are not in equilibrium or even far away from it, even if the chromatographic separation is performed at low velocity. Several examples of such systems will be shown and methods to overcome limitations in chromatographic processing will be discussed.

10:30 Coffee Break in the Exhibit Hall. Last Chance for Poster Viewing.
Next, we will discuss the continuous isolation of Extracellular vesicles, more particularly exosomes, as nanostructures of great medical interest. Similar to other complex biopharmaceuticals such as viruses, the purification of these nanostructures is still a considerable challenge. Here we describe an efficient and scalable purification strategy based in multi-column chromatography.
Present a poster and save €45!

Share your Data and Discover the Latest Advances in Bioprocess Research in the Exhibit Hall

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by 1 February 2019.
 Monday, 18 March

13:00 - 16:00 Recommended Short Course*
SC2: Potency Assays for Cell and Gene Therapies
*Separate registration required, see page 5 for details.

Tuesday, 19 March

7:00 Registration and Morning Coffee

REGULATORY AND CMC REQUIREMENTS

8:25 Chairperson’s Opening Remarks
Christopher Bravery, PhD, Consulting Regulatory Scientist; Consulting on Advanced Biologicals Ltd.

9:00 Regulatory Strategies for Cell and Gene Therapies
Vicky Coutinho, PhD, Senior Director, Regulatory Affairs, Autolys

Cell therapies are inherently more complex than standard biologics or new chemical entities. This presentation aims to address specific nuances for a cell therapy Investigational New Drug (IND) application and non-clinical considerations. An overview of the different expedited programs will also be reviewed.

9:30 KEYNOTE PRESENTATION: GMP for ATMP Manufacturing: An Industry Experience with Kymriah
Florence Salmon, PhD, Director Regulatory Affairs CMC, Novartis Pharma AG

Advanced therapy medicinal products (ATMP) are an emerging class of innovative biopharmaceutical medicines. Using Kymriah as an example, this presentation aims to provide an insight into the GMP requirements for ATMP manufacturing.

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

10:45 Developing Manufacturing Processes for the Production of Gene-Edited Allogeneic CART-Cells
Jean-Charles Epinat, PhD, Head of Process Development, Cellectis

Gene-editing has enabled off-the-shelf allogeneic CAR-T product candidates to reach the clinic. It is also endowing engineered cells with multiple new features, enhancing their capabilities and functions to better address cancer. Hindsight in industrializing these immuno-oncology products and the human clinical experience with the first cases in ongoing trials signal practical avenues for their further deployment and shed light on the transformative role they will play in the anti-cancer arsenal.

11:15 Developing Manufacturing Processes for the Production of Gene-Edited Allogeneic CART-Cells
Jean-Charles Epinat, PhD, Head of Process Development, Cellectis

Gene-editing has enabled off-the-shelf allogeneic CAR-T product candidates to reach the clinic. It is also endowing engineered cells with multiple new features, enhancing their capabilities and functions to better address cancer. Hindsight in industrializing these immuno-oncology products and the human clinical experience with the first cases in ongoing trials signal practical avenues for their further deployment and shed light on the transformative role they will play in the anti-cancer arsenal.

11:45 Sponsored Presentation (Opportunity Available)

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

12:45 Session Break

SCALE UP, AUTOMATION AND PROCESS CONTROL

13:30 Chairperson’s Remarks
Paula M. Alves, PhD, CEO, IBET; Director Animal Cell Technology Unit, ITQB NOVA

13:35 Next-Generation Bioprocess Development for Lineages Derived from Pluripotent Stem Cells
Robert Deans, PhD, CTO, Bluerock Therapeutics

14:05 Improving Functional Maturation of Human Pluripotent Stem Cells Derived Cardiomyocytes through Metabolic Understanding
Paula M. Alves, PhD, CEO, IBET; Director Animal Cell Technology Unit, ITQB NOVA

In vitro differentiation of human pluripotent stem cells into cardiomyocytes (hPSC-CMs) is a crucial process to enable their application in cell therapy and drug discovery. Despite the remarkable efforts towards the optimization of cardiac differentiation protocols, generated hPSC-CMs are still immature, closely reminiscent of fetal cardiomyocytes. In this study, we aim to overcome this hurdle by devising a novel metabolic-based strategy to improve hPSC-CMs generation and functionality. Noteworthy, we integrated structural and functional analyses of hPSC-CM with powerful "omics" technologies (proteomics, transcriptomics, metabolomics and fluxomics) as complementary analytical tools to support process optimization and product characterization.

14:35 Controlling Cell and Gene Therapy Manufacture through PAT
Damian Marshall, PhD, Head, Analytical Development, The Cell and Gene Therapy Catapult

Developing reliable, cost-effective processes for cell and gene therapy manufacture is a significant challenge. For autologous products, this challenge can be even greater due to the variability of the
patient-specific starting material and the lack of real-time process data. In this presentation we will show how optical biosensors can be applied for process monitoring to track cell behavior and gain higher level process control.

15:05 Refreshment Break in the Exhibit Hall with Poster Viewing

15:45 Closed System Manufacturing for Adaptive T-Cell Therapies
Ali Mohamed, PhD, Vice President, CMC, Immatics
Immatics developed a proprietary tumor antigen targets discovery platform which identifies novel tumor-specific targets and TCR candidates. It also screens TCR candidates based on these targets against off-target toxicities in absence of reliable in vivo models. Extensive process development was carried out using primary T cells derived from multiple healthy donors and cancer patients to optimize each step in the manufacturing of TCR T cells for 3 clinical trials (IMA101, IMA201, IMA202, and IMA203). Manufacturing for engineered TCR T cell therapies has been adapted into 3 different closed systems for future phases of clinical trials with excellent results.

16:15 Large Scale Production of LV and RV Vectors for T- and CD34+ Cells Transduction
Giuliana Vallanti, PhD, Director, Development & Quality Control, Qualified Person, MolMed
Lentiviral vectors (LV) and retroviral vectors (RV) are important starting materials used in gene therapy studies. A manufacturing challenge is the optimization of vector production in large-scale platforms. In MolMed we are developing two different LV/RV production systems using Pall iCELLis® fixed-bed disposable bioreactors. Full scale runs in Pall iCELLis bioreactor were already performed and results modeling the number of patients that can be treated with a single batch of vector will be presented.

16:45 Breakout Discussion Groups
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges. Then continue the discussion as you head into the lively exhibit hall for information about the latest technologies.

17:30 Welcome Reception in the Exhibit Hall with Poster Viewing

Wednesday, 20 March

8:00 Registration and Morning Coffee

IMPROVING SCALE AND PRODUCT CONSISTENCY
8:25 Chairperson's Remarks
Manuel Carrondo, PhD, Professor of Chemical and Biochemical Engineering, FCT-UNL, Vice President, IBET

8:30 Early COGS Evaluation as a Tool for Process Design and Planning: The Case of Allogeneic Cell Therapy for Bone Defects
Benoit Champluvier, PhD, Chief Technology and Manufacturing Officer, Bone Therapeutics, Belgium
This presentation will examine cell therapy solutions for bone defects and spinal fusion procedures. Future manufacturing process shall deliver products with a sustainable cost/benefit. COGS analysis early in the projects is key to define the process development strategy. Advantages and limitations of early COGS assessment will be discussed.

9:00 Safety and Efficiency of Viral Genes for Cell Therapy
Rolf Werner, PhD, Professor, University of Tuebingen

9:30 Engineering Scalable Manufacturing of High-Quality Human MSC for Cell Therapy: From Up to Downstream Processing Integration to Cell Proteome Characterization
Margarida Serra, PhD, Senior Scientist, iBET- Instituto de Biologia Experimental e Tecnológica
The aim of our work was to prove the scalability of an integrated bioprocess compatible with current good manufacturing practices (cGMP) comprised by cell expansion, harvesting, volume reduction and washing unit operations using human mesenchymal stem cells (hMSC) isolated from bone marrow and adipose tissues. Single-use technologies were adopted at different steps of the manufacturing workflow to support process integration and scale-up. Alongside the standard quality assays for evaluating hMSC’s CQA, a proteomics workflow based on mass spectrometry tools was established to characterize the impact of processing on hMSC’s CQA.

10:00 Sponsored Presentation (Opportunity Available)

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

Plenary Session: NEXT-GENERATION PROCESSES AND PRODUCTS
11:15 Chairperson's Remarks
Manuel Carrondo, PhD, Professor of Chemical and Biochemical Engineering, FCT-UNL, Vice President, IBET

Stefanos Grammatikos, PhD, Vice President, Head, Biotech Sciences, UCB Pharma
Current trends in clinical development acceleration and bioprocess intensification impose an unprecedented compression of CMC development timelines and new bioprocessing challenges downstream of the cell culture bioreactor. In this talk I will present a series of innovations we have introduced, some incremental and some potentially disruptive, in an effort to avoid further complications while rising to the latest challenges of bio CMC development and bioprocessing.

11:50 Opportunities and Challenges in CAR T Manufacturing
Markwin Velders, PhD, Vice President, Operations, Managing Director, Kite Pharma EU B.V.
Update on the status of CAR-T development for use in the treatment of cancer. The success story of this paradigm shift and the challenges and opportunities that lay ahead for this therapy will be presented and discussed.

12:20 End of Conference

12:30 Bridging Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own
Wednesday, 20 March

10:00 Registration Open
10:30 Coffee Break in the Exhibit Hall with Poster Viewing

Plenary Session: NEXT-GENERATION PROCESSES AND PRODUCTS
11:15 Chairperson's Remarks
Manuel Carrondo, PhD, Professor of Chemical and Biochemical Engineering, FCT-UNL, Vice President, IBET

Stefanos Grammatikos, PhD, Vice President, Head, Biotech Sciences, UCB Pharma
Current trends in clinical development acceleration and bioprocess intensification impose an unprecedented compression of CMC development timelines and new bioprocessing challenges downstream of the cell culture bioreactor. In this talk I will present a series of innovations we have introduced, some incremental and some potentially disruptive, in an effort to avoid further complications while rising to the latest challenges of bio CMC development and bioprocessing.

11:50 Opportunities and Challenges in CAR T Manufacturing
Markwin Velders, PhD, Vice President, Operations, Managing Director, Kite Pharma EU B.V.
Update on the status of CAR-T development for use in the treatment of cancer. The success story of this paradigm shift and the challenges and opportunities that lay ahead for this therapy will be presented and discussed.

12:20 Session Break

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

13:00 Session Break

MEETING REGULATORY AND ANALYTICAL STANDARDS
13:40 Chairperson's Opening Remarks
Christine Le Bec, PhD, Head of CMC Analytical, Technology Development, Genentech

13:45 KEYNOTE PRESENTATION: LIUTURNA (voretigene neparvovec): From Clinical Development to FDA Approval
Dan Takefman, PhD, Head, Regulatory Affairs, Spark Therapeutics

14:15 Viral Vector Manufacturing and Control: Regulatory Considerations and Challenges
Matthias Renner, PhD, Scientist, Federal Institute for Vaccines and Biomedicines, Paul Ehrlich Institute
In respect to manufacturing and quality control, viral vectors are considered to be one of the most complex medicinal products. Regulatory aspects considering the fundamental steps in manufacturing and control of these medicinal products will be presented, and the regulatory framework for these products which are classified in the EU as advanced therapy medicinal products and are regulated centrally by the European Commission and the European Medicines Agency will be given.

14:45 Understanding the Effect of Post-Translational Modifications of AAV Capsid Proteins and their Impact on AAV Infectivity
Lin Liu, PhD, Principal Scientist, Bioanalytics Characterization, Biologics Development, Sanofi
Viral capsid proteins play an important role in cellular targeting and trafficking as part of the viral infection cycle, and thus any changes in the viral capsid protein sequence or post-translational modifications (PTMs) might impact viral targeting and infectivity. We evaluated the role of AAV capsid protein PTMs on AAV transduction potential by generating AAV2 and AAV5 capsid mutants and performing a stress study.

15:15 Analysis of Purity and Packaging of Gene Therapy Vectors and VLPs to Support Process Development Decision
Vanessa Carvalho, Senior Scientist, Electron Microscopy Services, Vironova
Challenges with scale up of gene therapy processes include surprises in purity profiles. Robust analytical solutions are required to avoid late surprises. Transmission electron microscopy (TEM) provide unmatched insights in characterization of viral gene vectors. MiniTEM automatically provides: comparative metrics on purity profiles of viral particle samples; automatically differentiates intact viral particles from process related impurities; correlation between potency and viral particle morphology.

15:45 Refreshment Break in the Exhibit Hall with Poster Viewing

16:25 Analytical Approaches to Characterize AAV Gene Therapy Products
Christine Le Bec, PhD, Head, CMC Analytical, Technology Development, Genentech
In recent years, AAV vectors have been increasingly evaluated in various gene therapy clinical trials. To sustain this, reliable, fast, robust, GMP compliant analytical methods and characterization protocols are needed. Specific analytical assays were performed to assess vector productivity, vector purity, potency and safety. I will present different methods to quantify host cell DNA and host cell protein to support the process development and characterize preclinical and clinical lots.

16:55 Looking at the AAV Particles from Inside and Outside Using Novel Analytical Tools
Eduard Ayuso, DVM, PhD, Team Leader, Innovative Vectorology; Scientific Director Translational Vector Core (CPV), Translational Gene Therapy for Genetic Disorders, Inserm, University of Nantes
Our laboratory has been deeply involved in the harmonization of adenov-associated viral vector (AAV) characterization through the international reference standard efforts and has developed novel protocols
for accurate titration of these vectors. Moreover, recent analytical tools based on next generation sequencing technologies, allowed us to identify and quantify residual DNA species in vectors produced in mammalian and insect cells. More recently, we have detected the presence of miRNA in the final product (i.e. after purification) of AAV vectors. Our examples show that it is crucial to push vector analytics forward to drive innovation in manufacturing processes and vector design.

17:25 Creating Sustainable Process Development Strategies for Gene Therapy Products
Barbara Kraus, PhD, Head, Gene Therapy Process Development and Technical Services, Shire

17:55 End of Day

18:00 Dinner Short Course Registration
See page 5 for details.

18:30 - 21:00 Recommended Short Course*
SC4: CMC Clinic: Where Am I Now and Where Do I Need to Be with My Dossier
*Separate registration required, see page 5 for details.

Thursday, 21 March

8:00 Registration and Morning Coffee

MANUFACTURING VIRAL VECTORS AT SCALE

8:25 Chairperson’s Opening Remarks
Mercedes Segura, PhD, Director, Next Generation Platforms and Technologies, bluebird bio

8:30 FEATURED PRESENTATION: Challenges in Process Scale Up with 500 L Scale Manufacturing of AAV
Marian Bendik, PhD, Site Lead Orth, Gene Therapy Center Austria, Biologics Operating Unit, Technical Operations, Shire
The presentation will provide overview of major manufacturing challenges associated with process scale up of transient HEK293 transfection together with downstream pitfalls. Further, it will sum up 3 years of manufacturing experience in AAV 500 L scale. What are unknown unknowns?

9:00 Process Development Strategies: Academic to CMO vs. Integrated
Jean-Philippe Combal, PhD, Co-Founder and CEO, Vivet Therapeutics
Vivet Therapeutics is a gene therapy company dedicated to the development of gene therapy treatments for inherited liver disorders with high unmet medical need. The company’s development strategy is to target the liver with a novel synthetic adeno associated virus (AAV-Anc80) to introduce therapeutic genes to hepatocytes. This presentation will discuss the internal vs. external manufacturing decisions gene therapy companies have to make on the road to commercialization.

9:30 Providing Tailored Solutions to Turn Ideas into Tomorrow’s Medicines
Raquel Fortunato, PhD, CEO, GeniBet Biopharmaceuticals
GeniBet is a GMP biopharmaceutical CDMO offering highly specialized microbial, cell culture and viral process development and GMP manufacturing services to research groups, biotech and pharma companies. GeniBet mission is to manufacture safe and reliable breakthrough products to support worldwide customers on building the therapies of the future.

10:00 Process Development Approaches for AAV Gene Therapy Products
Laurence Gurianvarch, PhD, Head, Upstream Development, Genethon
In recent years, AAV vectors have been increasingly evaluated in various gene therapy clinical trials. To sustain this, reliable, fast, robust, GMP compliant process development strategies are needed. I will present the technologies, tools and strategies employed during process development and scale up for an internal project.

10:30 Coffee Break in the Exhibit Hall. Last Chance for Poster Viewing.

11:15 Process Development Challenges in Gene Therapy Moving from Early Clinical to Late Phase/Commercial
Tarik Senussi, Head, Process Development, Gyroscope Therapeutics
Material to supply initial clinical studies is often delivered via early stage contract manufacturing organisations to clinical phase appropriate regulatory standards. This inevitably requires subsequent modification and transfer to a facility that can support late stage and commercial manufacture as the product progresses through development. This talk will cover the opportunities and challenges associated with this transition, considering robustness, yield and comparability.

11:45 Vector Design and Production Scale-Up of AAV-Based Gene Therapies for Inflammatory Disease
Janneke Meulenberg, PhD, MBA, CIO, Arthrogen
Arthrogen is developing local gene therapy for inflammatory diseases, using viral mediated gene transfer. Arthrogen’s first product that has been tested in clinical trials, is an AAV5 based vector expressing interferon beta from an inflammation inducible promoter. This vector was produced using classical plasmid transfection in adherent cells. Arthrogen is currently evaluating different scalable systems for future AAV production runs. The pros and cons of these systems and the consequences for product characterization and quality control will be discussed.

12:15 Manufacturing Strategies and Regulatory Considerations for mRNA Therapeutics
Andreas Kuhn, Vice President, RNA Biochemistry & Manufacturing, BioNTech RNA Pharmaceuticals GmbH
Messenger (m)RNA is increasingly investigated as a platform technology for multiple therapeutic applications. This approach is most advanced in the context of immunotherapies against cancer, but is in general applicable whenever expression of a protein is desired. In my talk I will present the advantages and challenges for manufacturing mRNA for clinical studies. In addition, I will discuss regulatory considerations with respect to the classification of mRNA as gene therapy by both FDA and EMA.

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

13:15 Session Break

LENTIVIRAL PROCESS DEVELOPMENT

13:45 Chairperson’s Remarks
Mercedes Segura, PhD, Director, Next Generation Platforms and Technologies, bluebird bio

13:50 Bioprocessing Strategies for Gene Therapies
Mercedes Segura, PhD, Director, Next Generation Platforms and Technologies, bluebird bio
14:20 **Lentipro Stable Producer Cells for the Development of Scalable Lentiviral Vector Manufacturing**

Ana Sofia Coroadinha, PhD, Lab Head, Health & Pharma Division, Animal Cell Technology Unit Cell Line Development and Molecular Biotechnology Lab, IBET

This work discusses the challenges in lentiviral vector manufacture and scale-up as well the strategies and novel technologies to be adopted to enable effective upstream processes. At upstream, many of the challenges are related to the vector cytotoxicity, restricting the bioreaction to short-term productions. Thus, one of our strategies is to reduce vector cytotoxicity which enabled to establish lentiviral vector producer cell lines constitutively producing infective virus over 1 week.

14:50 **Lentiviral Vector Manufacturing - Problem or Not?**

Hanna Lesch, PhD, Director, Gene Therapy Unit, Kuopio Center for Gene and Cell Therapy

There are very few lentivirus success stories. Partially that has been explained because of the manufacturing issues. Is it still today a problem or are there solutions available? The talk will cover the main challenges, case study of process development and scale-up of lentivirus manufacturing into iCELLis500 and will dive into the future visions and possibilities.

15:20 **Close of Conference**
CAMBRIDGE HEALTHTECH INSTITUTE Training Seminars offer real-life case studies, problems encountered and solutions applied, along with extensive coverage of the academic theory and background. Each Training Seminar offers a mix of formal lecture and interactive discussions and activities to maximize the learning experience. These Training Seminars are led by experienced instructors who will focus on content applicable to your current research and provide important guidance for those new to their fields.

**Tuesday 19 March & Wednesday 20 March**

Day 1: 08:25 - 17:30 | Day 2: 8:30 - 12:20

**TS1: DESIGN OF EXPERIMENTS FOR BIOPROCESS ANALYSIS**

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

**Instructor:**
Marcello Fidaleo, PhD, Associate Professor, University of Tuscia; Teaching Fellow, Biomanufacturing Training and Education Center, North Carolina State University

**TRAINING SEMINAR INFORMATION**

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

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

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

CHI OFFERS COMPREHENSIVE SPONSORSHIP PACKAGES that can be customized to your company’s objectives and budget. Sponsorship allows you to achieve your objectives before, during, and long after the event. Packages may include podium presentations, exhibit space and branding, as well as the use of delegate lists. Signing on early will maximize your exposure to qualified decision-makers and drive traffic to your website in the coming months.

PODIUM PRESENTATIONS Available within the Main Agenda!
Showcase your solutions to a guaranteed, targeted audience through a 15- or 30-minute podium presentation during a specific conference program, breakfast, lunch, or separate from the main agenda within a pre-conference workshop. Package includes exhibit space, on-site branding, and access to cooperative marketing efforts by CHI. For the luncheon option, lunches are delivered to attendees who are already seated in the main session room.

INVITATION-ONLY DINNER/HOSPITALITY SUITE
Select specific delegates from the pre-registration list to attend a private function at an upscale restaurant or a reception at the hotel. From extending invitations, to venue to suggestions, CHI will help you obtain more targeted, quality leads throughout the year. We will mine our database of over 800,000 life science professionals to meet your specific needs. We guarantee a minimum of 100 leads per program! Opportunities include:

• Conference Tote Bags
• Literature Distribution (Tote Bag Insert or Chair Drop)
• Badge Lanyards
• Program Guide Advertisement
• Conference Notebooks and more...

EXHIBIT
Exhibitors will enjoy facilitated networking opportunities with qualified delegates, making it the perfect platform to launch a new product, collect feedback, and generate new leads. Exhibit space sells out quickly, so reserve your booth today! Due to limited space exhibits are available only through sponsorship.

ADDITIONAL OPPORTUNITIES AVAILABLE FOR SPONSORSHIP INCLUDE:

• Conference Tote Bags
• Literature Distribution (Tote Bag Insert or Chair Drop)
• Badge Lanyards
• Program Guide Advertisement
• Conference Notebooks and more...

LOOKING FOR ADDITIONAL WAYS TO DRIVE LEADS TO YOUR SALES TEAM?
CHI’s Lead Generation Programs will help you to obtain more targeted, quality leads throughout the year. We will mine our database of over 800,000 life science professionals to meet your specific needs. We guarantee a minimum of 100 leads per program! Opportunities include:

• Whitepapers
• Webinars
• Custom Market Research Surveys
• Podcasts
• Executive & Director
• Manager
• Professor
• Assistant

2018 SPONSORS

• Applikon Biotechnology
• Bilfinger Industrietechnik Salzburg GmbH
• Caprion Biosciences Inc.
• cytensa GmbH
• Flownamics, Inc.
• Halo Labs
• Hamilton Bonaduz AG
• Hovione SA
• JSR Life Sciences
• Labor Dr. Merk & Kollegen GmbH
• MERCK
• METTLER TOLEDO AUTOCHEM
• NanoTemper Technologies
• Oviozo
• Pall FortéBio
• Polysaccharide Adhesives
• Porton Biopharma Ltd
• RESOLUTION Spectra Systems
• Sartorius Stedim Biotech
• Shimadzu Europa GmbH
• Valitacell

For more information regarding sponsorship packages or the conference, please contact:

COMPANIES A-K:
Sherry Johnson
Sr. Business Development Manager
781-972-1359
sjohnson@healthtech.com

COMPANIES L-Z
Carolyn Cooke
Business Development Manager
781-972-5412
ccooke@healthtech.com