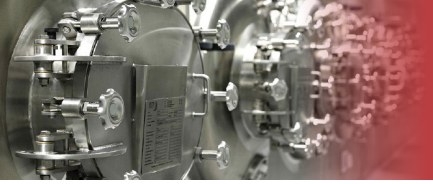

BioTalk EU
Biological Manufacturing Excellence

20th - 21st September 2023
Berlin, Germany
Global Manufacturing Strategies

DAY ONE

07.45 - 08.30 REGISTRATION

08.30 - 08.40 WELCOME & CHAIRPERSON'S OPENING REMARKS FOR DAY ONE
Dr. Uwe Gottschalk, Operating Partner, **Keensight Capital**

08.40 - 09.10

Smart Process Analytics for the End-to-End Batch Manufacturing of Monoclonal Antibodies
- For many modern biopharmaceutical processes, manufacturers develop data-driven models using data analytics/machine learning (DA/ML) methods. The challenge is how to select the best methods for a specific dataset to construct the most accurate and reliable model. This article describes the application of smart process data analytics software to industrial end-to-end biomanufacturing datasets for monoclonal antibody production to automate the determination of the best DA/ML tools for model construction and process understanding. The application demonstrates that smart process data analytics software captures product-and process-specific characteristics for two different monoclonal antibody productions. This study provides tools that can be widely applied to biomanufacturing processes for root cause analysis, prediction, and control.

Moo Sun Hong, Assistant Professor, Laboratory of Advanced Manufacturing Process (LAMP), **Seoul National University**

Downstream Processing

09.10 - 09.40

Next generation downstream processing
- High throughput process parameter screening to speed up development timelines
- Downstream process intensification to increase facility utilization
- CFD and mechanistic modelling to support scale-up from small scale to final commercial scale

Harald Bradl, Director and Head of Protein Science, **Boehringer Ingelheim**

09.40 - 10.10

Insights into Platform Purification Process Evolution
- Using initial capture as an example, look at current landscape of purification options available and how to evaluate
- Consider if non Protein A option(s) may be useful to integrate into a DSP development toolbox
- Making effective use of process and cost models, within DSP development, to support decision making
- Impact of covid pandemic on purification development

Graham McCartney, Director EU Operations, **Samsung Bioepis**

Upstream Processing

Raman spectroscopy to stabilize product quality for continuous upstream processes
- Today's pharmaceutical industry has a high interest in moving towards continuous biomanufacturing
- Continuous processes based on cell culture perfusion become highly attractive for mAbs
- The bioprocess footprint is reduced by running a smaller bioreactor in steady-state perfusion during weeks/months
- Keeping a process in a steady state despite culture aging demands a tight feedback control system
- This case study shows the power of Raman to stabilize the process

Martin Jordan, Senior Scientist, **Merck**

Effective cell culture operations by accurate, non-invasive determination of the critical process parameter pH in Roche`s Drug Substance Network
- Problem statement: Limitations of the current industry standard of sample based offline pH measurement
- Solution: BioTalk 2018 Follow up on offgas based pH determination: how it works
- Manufacturability: Implementation of the offgas based reference method in GMP manufacturing
- Results: Some thoughts on business value
- Take home messages / Discussion starters

Christian Klinger, Senior Expert MSAT Process Science & PTT Global MSAT DS EU/APAC, **Roche**

10.10 - 11.00 COFFEE BREAK & MEETINGS

11.00 - 11.30

Introducing Planova™ S20N, a Novel Superior Regenerated Cellulose Virus Removal Filter
- Made of superior cuprammonium regenerated cellulose NEW PLANOVA S20N withstands higher operating pressure making it simple for the post-use integrity test.
- Planova S20N shows robust virus removal capability, higher throughput, and stable protein filterability at higher operating pressures over a wider range of solution conditions and molecules (e.g., multi-specific antibodies).
- We will present the characteristics and results of customer-led evaluations and internal studies on Planova S20N filters.

11.30 - 13.00

One to One Meetings
- Downstream/Upstream Process Technology Platforms
- Digitalization
- Specialised cell culture media
- Single-use & Disposable Technologies
- Separation and Purification Technology
- Virus Filtration Processes
- Smart Manufacturing Technologies – Tech. Transfer
- Facility Management & Integration
- Biopharma & Modular Biosafety Technology
- Capacity & Facility Design
- Multi product facilities
- Fluid Management Systems
- Lean/Operational Excellence
- Continuous Improvement
- PAT & MES, Automation and Process Control Excellence
- QbD, Quality Assurance & Quality Systems
- Validation Process/Life cycle Management systems
- Regulation – Rapid Release Testing
- cGMP – Contract, External Manufacturing Services
- Biogenerics/Biobetters
- Personalised Medicines
- Cell & Gene Therapy
- Fill and finish
- Microbial Process Development and Production

11.30 - 12.00

Filling the gap between Downstream & Fill-Finish with scalable single-use technologies
- The advantages of bags over bottles for primary packaging
- Eliminate manual processes during substance filling
- Benefits of controlled plate-freezers for your product quality

12.00 - 12.30

Understand Manufacturing Costs, Impact on Yield and Sustainability of Single-use Technologies in Bioprocesses by Modelling
- In this presentation we will examine the impact of process intensification on sustainability and cost saving opportunities and yield improvements through advanced material solutions.
- Advanced material-based technologies offer the ability to intensify processes by enabling faster mass transfer, being able to operate in a broader range of conditions and deal with a diverse range of particle sizes.
- In a case study we will compare advanced single-use technologies with more traditional approaches and show the impact on cost savings and sustainability.

12.30 - 13.00

Accelerating upstream process development with direct CQA and media analysis feedback
- Informed decisions are made faster by consolidating at-line CQA and culture media analytical testing, with the combination of Sartorius Ambr 15 and Waters BioAccord LC-MS systems.
- Day-to-day changes in CQAs, like glycosylation, and the impact of process parameter variations can be tracked at-line by process engineers.
- Close-coupled feedback allows CQAs to drive process parameters. Cell culture media are analyzed at-line throughout clone selection and process development activities.
- Statistical analysis tools can be applied to gain insight on key metabolic changes.

13.00 - 13.50 NETWORKING LUNCH

Downstream Processing

Upstream Processing

13.50 - 14.20

Development of Process Analytical Technologies for Downstream Processing in Commercial Biologics Production
- Examples of PAT application in DSP manufacturing process
- Benefits and challenges of inline measurements and controls in GMP production.

Martyna Kielmas-Palach, Manufacturing Scientist, **Biogen**

PAT in Upstream Processes – Fantastic as Development Tool and When to Use in Manufacturing
- Examples of PAT tools used in USP development and transfer
- Raman spectroscopy for generic plattform-wide prediction models
- Biocapacitance for precise CSPR control in N-1 perfusion development
- Multidimensional Fluorescence spectroscopy in media preparation
- Online measurement of oxygen uptake rates to support clone selection
- When should PAT move from development to manufacturing

Nicolas Maguire, Late Stage Upstream Process Development Scientist, **Boehringer-Ingelheim**

14.20 - 14.50

Process Intensification technologies using In-line concentrators for High Titer mAb process
- As mAb titers are increasing, its straining downstream purification manufacturing technologies. One of the issues facing manufacturing is the ever increasing in-process volumes, due to increasing titers.
- In this case study we would look at comparative evaluation of Single Pass Tangential flow filtration (SPTFF) or In-line product concentrators technologies for the there management of in-process volumes for downstream process fit.
- Comparative evaluation of SPTFF technologies on in-process volume controls including process robustness and controlling parameters, product quality impact, manufacturing scalability and implementation

Sanjay Nilapwar, Principal Scientist/Group Leader, **AbbVie**

Superior cell culture performance through rational media design
- Continuous improvement of chemically defined media for efficient and robust antibody production of CHO cell lines
- Enhanced media insights from metabolic and in silico methods
- Enabling high titer, high viability process starting from FIH
- Media design and feeding strategy modulation to target productivity and product quality

Dr. Sarwat Khattak, Head Of Cell Culture Development, **Biogen**

14.50 - 15.20

Realization of automated learning for bioprocess development by integrating robot-driven well-controlled parallel cultures, analytical technologies, and modelling
- Automated laboratories become state of the art. However, to gain a maximum of knowedge from the experiments, implementation of a closed loop learning framework is a key with (i) integrated real-time high-throughput analytics, (ii) proper automated real-time handling of the generated data to control the running experiments. The data should follow the FAIR (Findable Accessible Interoperable Reusable) principles, (iii) Integration of a model-based tool tailored for the small data problem, real-time use of mathematical models that can deal with the low data/complexity ratio that characterizes bioprocess development.
- The KIWI-biolab aims to solve these issues with an integrative and collaborative approach. Analytical technologies are connected with high throughput cultivation systems and with tools for automated documentation and standardization of experimental/computational workflows. AI approaches are adapted to High Throughput Bioprocess Development by the use of mechanistic models in combination with Machine Learning algorithms (hybrid models). The strength and relevance for scalability of this approach is documented by examples from bacterial protein expression projects.

Prof. Dr. Peter Neubauer, Chair of Bioprocess Engineering, **Technical University of Berlin / TU Berlin**

15.20 - 16.10 **COFFEE BREAK & MEETINGS**

16.10 - 17.10

One to One Meetings
- Downstream/Upstream Process Technology Platforms
- Digitalization
- Specialised cell culture media
- Single-use & Disposable Technologies
- Separation and Purification Technology
- Virus Filtration Processes
- Smart Manufacturing Technologies – Technology Transfer
- Facility Management & Integration
- Biopharma & Modular Biosafety Technology
- Capacity & Facility Design
- Multi product facilities
- Fluid Management Systems
- Lean/Transformational Change – Operational Excellence
- Continuous Improvement / Manufacturing Processing
- PAT & MES, Automation and Process Control Excellence
- Quality Assurance, Quality Systems QbD
- Validation Process/Life cycle Management systems
- Regulation – Rapid Release Testing
- cGMP – Contract, External Manufacturing Services
- Biogenerics/Biobetters
- Personalised Medicines
- Cell & Gene Therapy
- Fill and finish
- Microbial Process Development and Production

16.10 - 16.40

Advances in Protein A Chromatography Resins
- Jetting technology is a continuous emulsification technology by which all Praesto® chromatography resins are produced.
- This proprietary technology results in resins with a narrow, almost uniform particle size distribution, with excellent mass transfer properties.
- Herein, we present advances which utilize Jetting technology, including process intensification models and a novel Protein A resin designed specifically for elution of Fc-containing molecules at higher pH levels

16.40 - 17.10

How to Address GMP Annex 1 Requirements Implementing Single-Use Assemblies for Final Fill
- **Single-use systems in final filling: effects on efficiency and scalability**
- Significant updates in the New Annex 1 and their expectations regarding the use and control of single-use systems
- Annex 1 and final fill single use systems: synergy for greater compliance
- How molded closed single-use systems can reduce the risk of contamination, enhance efficiency, and ensure safety and quality

17.10 - 17.40

Industrialization of biotechnology process with continuous DSP approach

In 2020, demand for development and manufacturing of antiCOVID molecule exploded. This talk presents how LFB Biomanufacturing succeeded to reply to customer in an emergency context and supply shortage with DSP continuous solutions.
- Reuse of consumables and single Use chromatography Membranes
- On line Dilution and On line concentration
- Viral clearance studies
- Removal of centrifugation steps by filtration with diatomaceous earth

David Balbuena, Head of Process Development and GMP Manufacturing chez **LFB Biomanufacturing**

Design of Experiments and Modelling for Process Characterisation Studies
- DoE as a tool to optimise process characterisation studies
- Points of attention for the statistical analysis plan
- Acceptance criteria to define CPPs/PARs
- Case study from upstream process development

Alexandre Super, Statistician CMC Development, **UCB Pharma**

17.40 - 18.10

Strategy to develop and implement a Downstream Continuous Bioprocess with a fully integrated system for clinical manufacturing scale
- The equipment and automation supporting Next Generation Manufacturing (NGM) for downstream unit operations can be complicated and expensive. We present an integrated solution for chromatography column operation, viral inactivation with pH control, filtration and in-line dilution
- This solution can lead to significant reductions in facility size, manufacturing costs, and enhanced product quality when compared to the usual batch mode of operation, or the alternative to integrate many different pieces of equipment through a Distributed Control System (DCS) from different vendors
- Details of operation, for the duration of a perfusion run, with bioburden control are explained
- Implementation strategy for GMP manufacturing is presented

Irina Ramos, Director Downstream Continuous Manufacturing, Bioprocess Engineering & Technology Group, **AstraZeneca**

18.10 - 18.45

Open Panel Discussion: **Taking Bioprocess Innovation and Applying them Successfully to Other Modalities**
- Leveraging expertise in biologics to enable new modalities (gene therapy, cell therapy, etc.)
  - What have we learned that can be applied directly?
  - What are the unique challenges with viruses and allogeneic cell therapies?
- New technologies that improve biological understanding for manufacturing complex proteins (PAT tools, real time monitoring)
- Have these proven useful? What are the gaps and opportunities?
- Key challenges to get autologous cellular products to as many patients as possible (including solid tumor indications)

Moderator: **Dr. Uwe Gottschalk,** Operating Partner, **Keensight Capital**
Panel Members:
Roman Necina, General Manger, HOOKIPA Pharma Inc., **Ludek Sojka,** Chief Executive Officer, SCTbio,
Amir Goudarzi, Senior Director Bioprocess Technologies, Bayer

18.45 **CHAIRPERSON'S CLOSING REMARKS AND END OF DAY ONE**

18.50 **NETWORKING DRINKS RECEPTION**

Please note: agenda and speakers are subject to change

DAY TWO

08.15 - 08.20 **CHAIRPERSON'S OPENING REMARKS FOR DAY TWO AND SUMMARY OF DAY ONE**
Dr. Uwe Gottschalk, Operating Partner, **Keensight Capital**

08.20 - 08.50 **On the use of Process Analytical Technology (PAT) and Process Data Analytics (PDA) for Manufacturing Intelligence in batch and continuous bioprocessing**

- Manufacturing Intelligence focuses on the use of workflows, architecture, digital and manufacturing technologies for optimized process resources, enhanced decision making and process intervention strategies.
- PAT and PDA represent key enablers for manufacturing intelligence and digital bioprocessing
- Raman spectroscopy-based PAT can be applied for process design, understanding and automation via monitoring, control, and supervision in batch and continuous operations.

08.50 - 09.20 **The Convergence of Process Intensification, Automation and Analytics, and PAT to Enable Continuous Processing and Biopharma 4.0**

- In this talk we will present how the adoption of process intensification, PAT, advanced data analytics, and process monitoring provides the foundation for continuous bioprocessing. We will examine the benefits of:
- Combined and intensified process steps which increase process efficiency and reduce costs, all in a smaller footprint
- Software that automates data acquisition, aggregation, and provides visualization and analysis tools that supply the right data, at the right time for data-driven decision making
- PAT tools such as inline Raman spectroscopy and chemometric software allowing real-time monitoring of CPPs and CQAs for improved process control
- Orchestration software giving overall visibility, monitoring, and trending of unit operations across the process workflow

	Bioprocess Innovation	CMC Development
09.20 - 09.50	**Deployment strategies of Digital Twins for accelerating bioprocess life cycling** • Digital transformation is not an option • Digital Twins are a central part of the digital transformation • End to end digital twins decrease development efforts by 50% • Real time deployed digital twins allow for process robustness and optimization **Christoph Herwig,** Professor Biochemical Engineering, **TU WIEN**	**Challenges of a virtual Biotech company in outsourcing CMC development** • CMC development in a small virtual company • Outsourcing approaches of different CMC tasks • Early research oriented versus late IMPD oriented development tasks • CDMO contract generation, project and project management • How to put needed flexibility into CDMO contracts • Pitfalls to avoid in contract negotiations • Pros and Cons of 1-stop shop versus several specialized CDM**Os** **Berthold Boedeker,** CTO, **Tribune Therapeutics AS**
09.50 - 10.20	**Development of a monoclonal antibody using QbD approaches** • Development of a monoclonal antibody using QbD approaches • Iterative risk assessments to determine focus areas for experiments • Determination of potential Critical Process Parameters per purification stage • Design of Experiments during early and late stage to further understand behavior of process parameters • Use of statistical modeling, including Monte Carlo simulation, to develop the control strategy • Process performance qualification **Bas Kokke,** Principal Scientist Downstream Processing, **Byondis**	**Innovative analytical strategies for addressing common problems for new molecular format CMC development** • Complex next generation biological molecules are becoming increasingly prevalent in today's biopharmaceutical manufacturing landscape. Such molecules present unique challenges, due to their complex structures and heterogeneity, when compared with traditional antibody formats. Through case studies, this presentation will highlight innovative analytical strategies for addressing common problems during product development such as chain assembly, multiple-MoAs and diverse post-translational modifications **Ian Anderson,** Global Senior Principal Scientist, **Lonza**

10.20 - 10.45 **COFFEE BREAK & MEETINGS**

10.45 - 11.30 **Roundtable Discussions**
For 4 to 8 participants (per roundtable) to discuss and debate on a topic of their choice

1. Accelerating upstream process development – robust, scalable and reproducible process
2. Cell culture performance by rational media design and single-use bioreactors
3. Development of Continuous Purification Processes
4. Process Intensification, Automation, Analytics, and PAT to Enable Continuous Processing and Biopharma 4.0
5. Digitalisation and Automation for Acceleration of Bioprocess Development
6. Integration of Process Analytical Technologies in Downstream Process Control
7. Best Practices In CMC Development And Effective Technology Transfer

11.30 - 13.00

One to One Meetings

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- Regulation – Rapid Release Testing
- cGMP – Contract, External Manufacturing Services
- Biogenerics/Biobetters
- Personalised Medicines
- Cell & Gene Therapy
- Fill and finish
- Microbial Process Development and Production

11.30 - 12.00 **Optimizing Harvest and Recovery with Single Step Depth Filtration**

- Filter and diatomaceous earth selection
- High throughput screening at 20ml sample size
- Scalability from 0.1L to 2,000L+
- Scale-up for pilot and production

12.00 - 12.30 **Advances in Protein A Chromatography Resins**

- Jetting technology is a continuous emulsification technology by which all Praesto® chromatography resins are produced.
- This proprietary technology results in resins with a narrow, almost uniform particle size distribution, with excellent mass transfer properties.
- Herein, we present advances which utilize Jetting technology, including process intensification models and a novel Protein A resin designed specifically for elution of Fc-containing molecules at higher pH levels.

12.30 - 13.00 **The Evolution of Bioprocess Filtration Single Use Automation: From the Laboratory Bench to the Final Package**

- Why automating a single use bioprocess leads to increased process efficiency and reduces risks.
- How small-scale automation can be used to ensure scale up accuracy and filter performance at cGMP level.
- Automating bulk filtration and dispensing applications.
- The strategic benefits of automating this process.
- Automated NFF Systems – optimise, control and simplify NFF processes

13.00 - 13.50 **NETWORKING LUNCH**

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	Bioprocess Innovation	CMC Development
13.50 - 14.20	**Late-stage upstream process development: Studies and their timing** • Process characterization • Justification of process and microbial control • Hold time studies • Reprocessing **Deborah Hol,** Principal Scientist USP, **Byondis B.V.**	**From Development Through to Tech Transfer: Bridging latest High Throughput instrumentation with Legacy Instrumentation** • Comparability study using Ambr® 15 integrated with NovaFlexII against legacy instruments across the expected process ranges • Application of correction factors obtained from a Novaflex II integrated with Ambr® 15 to a Novaflex II integrated with Ambr®250 and final confirmatory study **Anagha Eswar,** Senior Scientist, **AstraZeneca**
14.20 - 14.50	**Implementation of a highly digitalized process architectures for biopharmaceutical development** • Highly digitalized process architectures for future biopharmaceutical development • Integrated process and analytics digitalization strategy speeds up PAT development • Integrated soft sensors and automation can aid minimizing human intervention and increasing process robustness • Choice of PAT sensor and control strategies affects modelling need **David-Benjamin Nickel,** Technical Lead, Modelling and Data Science, Technology Development and Implementation, **Takeda**	**The right process for the right CMC Needs: Could Upstream Process Toolbox & Process Modelling help to drastically increase DS Productivity** • Platform cell culture processes have several advantages over the case by case redevelopment of processes: seamless transfer of platform knowledge between products, process development acceleration, de-risk scale up and application of validated scale down models. • Nevertheless specific CMC projects have specific needs, met by integrating and applying specific cell culture changes • The current strategy and structure of UCB upstream process toolbox including modeling technics and focus on multiple case studies, from clone selection to harvest step. • Our toolbox methodology combined to process modeling technics provide a better insight into the impact of process parameters on production yields and product quality, thus improving process understanding and control as well as accelerating process development with a more flexible and agile strategy **Antoine Piednoir,** Senior Scientist, **UCB Pharma**
14.50 - 15.20	**Data-driven innovation in biotech manufacturing: advanced analytics to boost performance and commercial value** • Key aspects for successful D&D implementations • Data & Digital architecture in commercial biotech manufacturing • Examples from upstream and downstream processing • Role of "big data" analytics and visualization platforms in effective decision-making **Francisca Gouveia,** Innovation Data & Digital Lead, **Novartis Pharma SAS**	**Beyond Antibodies – A Transformation** • Transformation from antibody development to developing cell and gene therapies • Increasing complexity from new modalities • Reagents to support cell and gene therapy projects • Case-study: Developing a plasmid DNA process **Markus Eser,** Head of Development Analytics, **Bayer**
15.20 - 15.40	**COFFEE BREAK**	
15.40 - 16.10	**Filling the gap between Downstream & Fill-Finish with scalable single-use technologies** • The advantages of bags over bottles for primary packaging • Eliminate manual processes during substance filling • Benefits of controlled plate-freezers for your product quality	
16.10	**CHAIRPERSON'S CLOSING REMARKS**	
16.15	**CLOSE**	

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