ICB III WORKSHOP SESSIONS

Workshop 1: Increasing Speed to Clinic with Continuous Biomanufacture

Chairs: **Todd Przybycien**, Carnegie Mellon University, USA
Jon Coffman, Boehringer Ingelheim Pharma, USA

Many companies are considering changing from fed batch and discontinuous processing to perfusion, continuous and integrated processing for late stage molecules. This requires comparability studies, several rounds of optimization and process characterization studies focused not only on productivity and robustness, but also on product quality. It is largely focused on reducing COGs, CAPEX, and increasing NPV.

Why not implement a continuous and integrated platform from the beginning of a product's life cycle? Is a continuous and integrated process easier to develop? Is it more robust? Is it easier to transfer/scale? Most importantly, can we use continuous and integrated processing to increase the speed to clinical trials? Is time more important than money?

What are the advantages to perfusion, continuous and integrated processing in early stage? What attributes of these processes lend themselves to early stage? How would the length of the perfusion cycle impact the speed to clinic?

How can we develop continuous upstream with no effort and little time? Same with downstream? What is the role of PAT in development and manufacturing? What PAT methods would we use in development but not in manufacturing?

How does a continuous upstream benefit pre-clinical supply? Has anyone done perfusion with transient cells? Has anyone developed an integrated perfusion/capture step suitable for the small material needs for research?

Workshop 2: Evaluating Future Continuous Facility Design Concepts

Chairs: **Suzanne Farid**, University College London, United Kingdom
Michael Borys, Bristol-Myers Squibb, USA

The possibility of building fully integrated continuous bioprocess facilities is becoming closer to reality with recent advancements. Yet significant effort may still be required when planning and design for future continuous manufacturing facilities. In this workshop, we will discuss future facility design concepts and their impact on costs, timelines, and PAT/control requirements. We will also consider gaps, risks and opportunities with implementing continuous facility designs.

Some of the future continuous facility design concepts that we can consider during this portion of the workshop include:

1. *Multiple small scaled-out continuous facilities* v. large scaled-up continuous facility?
2. *Fully continuous* v. hybrid facilities?
3. *Ballroom* v. segregated continuous facility?

We will be tapping into your experiences and insights on these two core themes, addressing questions such as:

Theme 1: Vision and evaluation of future continuous facility designs

Pick one of the future facility design concepts and consider the following questions:

1. How will future continuous facility design concepts impact future facilities in terms of:
   a. Building cost
   b. COG
   c. Drug development and validation costs
   d. Comparability, tech transfer and filing costs
   e. Complexity and risk
   f. Flexibility

   How would you rank these criteria when making decisions about future facility design concepts?
   How do we weigh up investment and risk versus ROI for decision-making?

2. What is the vision for the degree of PAT and control strategies required for successful operation of continuous facility design concepts for commercial manufacture?

   What timeframe is required to reach this vision?

Theme 2: Gaps, risks and opportunities with implementing continuous facility designs

Pick one of the future facility design concepts and consider the following questions:

1. What gaps still exist for implementation of future continuous facility design concepts?
   Please consider manufacturing technologies, analytical technologies, QbD strategies, etc.

2. What are the greatest quality and regulatory risks and hurdles?
   What risk mitigation strategies can we adopt to de-risk implementation of continuous facilities?

Our goal is to facilitate a lively and interactive discussion where we encourage open dialogue and sharing of experiences from all participants. We will start with a quick check-in with participants for additional suggestions and prioritization of topics for the group to tackle. Please feel free to forward comments to us before the meeting.

Workshop 3: Gearing Up for Process Performance Qualification Readiness for ICB

Chairs: **Mark Brower**, Merck, USA
Jeff Salm, Pfizer, USA

Continuous manufacturing processes are not new to biotechnology. Several commercial biologic products include fully or partially continuous processes. These labor intensive processes were often created for instable products that were not amendable to batch processes. As the biotechnology industry continues to mature, companies are looking for more productive and efficient processes.

With several significant advances in technology, the biotech industry is experiencing a renewed interest in integrated and continuous manufacturing. This is furthered by indications from regulatory agencies that continuous processing can enable increased process control and product quality. As products made with these new approaches to manufacturing near the market, companies are realizing that traditional approaches to process validation may not be suitable.

In this workshop, we will discuss how process performance qualification differs for a batch versus integrated and continuous manufacturing processes. The goal of our session will be to determine a limited number of key areas for future engagement and industry leadership.

Potential topics to discuss include:

- How do we test failure modes and show a control strategy can accommodate process upsets?
- How do you test 'worst case scenarios'?
- Does the current '3 batch validation' approach work for ICB?
- Readiness for implementation: strategies for viral clearance, column monitoring, and start-up
- High reliance on automation and PAT (Testing of analytical equipment and feedback control)
- Monitoring, predicting process behaviour with MVA: How can we leverage MVA and how to develop and validate these models?
- Strategies for environmental monitoring, bioburden detection and response
- Are the proper tools in place to start PPQ runs: Risk assessments, protocols?
- Is new 'continuous' equipment up to GMP standards?

Workshop 4: Industry-Academia-Vendor-Government Collaboration in the ICB Space

Chairs: **Alessandro Butte**, ETH Zurich, Switzerland
Alex Xenopoulos, EMD Millipore, USA

Biopharma is still growing fast, yet changes in the business could happen even faster. Just to mention one, during the period 2009–2016 the expiration of patents for blockbuster drugs has reduced pharma's revenues in worldwide developed markets by US$127 billion annually, representing a 44% reduction in branded drug spending. This and other changes are putting an unprecedented pressure on big pharma to reduce cost of goods and to accelerate drug development. The theme of this conference is Integrated Continuous Biomanufacturing (ICB), asking whether ICB is the answer to reducing costs and timelines and looking for the best way to make its implementation a reality. The central question that will be debated during this workshop is whether a broad and close collaboration that involves all the different stakeholders is necessary to make ICB a reality. Is such "open innovation", not commonly used in our competitive industry, the only chance for biopharma to address the pressures? Does the biopharma industry need to "outsource" innovation in process development so as to free resources for what should be its core business, namely discovering and commercializing new drugs? Is the example of Lego, a company that went from losing more than $1 million per day in 2003 to double digit growth and more than 20% profit margin in the last five years through open innovation, the relevant example?

Experts from different fields will stimulate a discussion on how to promote innovation and the development of the required key enabling technologies in biomanufacturing and, more specifically, in continuous integrated manufacturing. What are the risks and the advantages of open innovation platforms, or of close partnerships like the one that will soon start between Oxford University and Novo Nordisk ($115 million in 10 years and more than 100 Novo Nordisk scientists on campus)? What is the role of vendors and of start-ups (or venture capital) in providing new technologies and manufacturing platforms? Would it be helpful to share data and standards, as is the case in the software industry? These and other questions will be addressed in groups, led by each of the experts, to promote discussion and sharing of experiences. The work of each round table will be summarized at the end of the workshop.