Program Overview – Sunday June 19 to Thursday June 23

Sunday	**AM**	Arrival (recommended: Saturday)	
	PM	**#1 The Origin of Impurities** - G. Vendantham, A. Amanullah	**Opening Keynote**
Monday	**AM**	**#2 Priorities in Cost & Performance Improvements** - D. Robbins, S. Ghose	**#3 The Marriage of HTS & Process Modelling** - M. Ottens, E. Broberg-Hansen
	PM	**Activities & Networking**	**Poster Session - Ocean of Innovation (1)** - Ch. Haynes, A. Lenhoff, D. Roush
Tuesday	**AM**	**#4 New Materials for Downstream Processing** - A. Zydney, M. Phillips	**#5 Purification from Platform to Diversity** - N. Tuğcu, D. Ambrosius
	PM	**Debates Sessions I / II / III (in series)** - N. Titchener Hooker, J. Curling	**#6 Purification of non-Protein Therapeutics** - H. Pujar, C. Heldt
		I: Continuous Processing, where should we be operating - K. Konstantinov, B. Kelley	
		II: Disruptive Technologies, why do they not seem to stick - H. Bak, J. Thömmes	**One Keynote every day!**
		III: Design of Experiments vs Modelling, show me the value - K. Łaçki, J. Hubbuch	
Wednesday	**AM**	**#7 Impact from Alternative Expression Systems** - S. Farid, L. Pampel	**#8 Process Challenges with Biosimilars** - S. Vunnum J. Myers
	PM	**Activities & Networking**	**Poster Session - Ocean of Innovation (2)** Ch. Haynes, A. Lenhoff, D. Roush
Thursday	**AM**	**#9 Increasing Patient Access to Biopharmaceuticals** - J. Coffman, B. Marques	**#10 Biomolecular Modelling for Manufacturability** - Ch. Dowd, P. Tessier
	PM	**#11 New Developments in PAT and QbD** - G. Ferreira, Th. Lemm	**#12 Next Generation Unit Operations & Integrated Processes** - J. Salm, J. Moscariello
Friday	**AM**	Departure	

Session 1 – Sunday afternoon, June 19

The Origin of Impurities

Session Chairs: Ashraf Amanullah and Ganesh Vedantham

Successful development and marketing of a therapeutic bioproduct requires control of process and product related impurities throughout the manufacturing process, but in particular drug substance. The vast majority of product quality attributes and impurities are associated with the host cell line and the upstream manufacturing process. These include but are not limited to aggregates, charge variants, host cell DNA, endotoxins, host cell protein and endogenous viruses. With advances in analytical techniques (e.g. high resolution mass spectrophotometry), very low levels of impurities can now be identified and quantified. Progress in the areas of functional genomics, cell line development and process engineering increases the probability of controlling the impurities at its sources. Smart Bioprocessing should include a rigorous assessment of how the upstream processes might be altered—perhaps even radically—to enable more efficient processes and more consistent product quality and purity.

We solicit thought provoking contributions in the area of identifying and controlling impurities at its origin, focusing on the following key questions:

- How can we leverage the advances in biology to control host cell associated impurities?
- Can we make product with little or no variants?
- What can be done to stabilize the product while in its intra- or extra-cellular environment?
- How does the product interact with other, non-product related impurities?
- How can we leverage genetic engineering to reduce the levels endogenous viruses?
- How can we utilize molecule/manufacturability assessment tools to support the selection of cell lines to generate the desired product quality and impurity profiles
- How can we alter the upstream manufacturing process to enable more consistent product quality and purity?

Session 2 – Monday morning, June 20

Priorities in Cost and Performance Improvements

Chairs: Sanchayita Ghose and David Robbins

With the maturation of the biotech industry and growing production requirements and cost pressures for biopharmaceuticals, there has been an increasing focus on lowering cost and improving productivity of our current and future manufacturing processes. This needs to be achieved while maintaining consistent control of product quality and process performance. A "smart bioprocessing" approach to setting priorities and making decisions is needed to enable development of high performing processes that also meet cost and demand requirements. In response to high mass requirements, significant strides have been made on the upstream side with high productivity cell lines, efficient media optimization, and high throughput operation modes such as perfusion bioreactors. As a result, many companies are now grappling with the issue to come up with creative solutions to prevent downstream from being the process bottleneck.
This session will showcase industrial case studies highlighting efficient and economic process design as well as use of new technologies that will pave the way for the next era of biomanufacturing.
Presentations are encouraged which address the following questions:

- How can a more systematic approach to understanding manufacturing bottlenecks and costs enable process developers and production facilities to work together more efficiently to deliver better integrated, more productive processes?
- What new approaches have been most successful in enabling facility fit to increase capacity in legacy facilities, or in delivering lower capital and operating costs in new, smaller, more efficient facilities?
- What challenges or opportunities do new manufacturing modes present for maintaining or improving control over product quality and process performance?
- How can the benefits of integrating all aspects of the process best be achieved?
- What are the real benefits of single-use technology? When should it be used and what are the challenges?
- How important are connected and continuous processing? How can they be used to the greatest benefit? What considerations inform the selection of the right technology?
- How can "behind the scenes" support functions (*e.g.*, buffer preparation, in-line dilution/mixing, column packing, cleaning, sanitization/sterilization) be optimized to remove hidden bottlenecks, increase productivity, and lower costs?
- How can the biopharmaceutical industry benefit from the lessons learned and solutions developed in other more mature manufacturing fields?

Session 3 – Monday morning, June 20

The Marriage of High Throughput Screening and Modeling

Chairs: Ernst Hansen and Marcel Ottens

Process development timelines can be reduced by combining High Throughput Screening (HTS) with Design of Experiments (DoE) to find robust operating points within the Quality by Design (QbD) paradigm. An even better process understanding can be obtained, if HTS is instead combined with mechanistic modeling, replacing the empiric method of DoE with models based on reaction and separation science. This model based approach allows us to predict and understand the behavior in a larger design space, even outside the experimental range. It is also an efficient and transparent way to share knowledge between similar steps in different processes. Recent trends also suggest that the ability to explain process behavior using a mechanistic model is welcomed by the FDA. In another approach, Quantitative Structure Property Relations (QSPR) modeling might aid in e.g. pre-selecting resins for certain separation tasks at hand. The marriage of HTS and Modeling combines the capacity of HTS with the increased process understanding of Modeling, and is therefore an ideal candidate to contribute to smart bioprocessing, the theme of this conference.

This session seeks contributions both from industry and academia where Modeling at different modes/scales, combined with HTS generated data improved process development (better output or shorter time). To unleash the full potential of the combination of HTS and Modeling we would like to see questions answered in this session, like:

- How should the HTS experimental workflow be scheduled to obtain the most trustworthy parameters for mechanistic modeling?
- How to get the most information out of limited sample volumes, limited time and resources?
- How can QSPR be effectively incorporated to guide the HTS workflow?
- How can advanced statistics combined with HTS help to improve process development?

Session 4 – Tuesday morning, June 21

New Materials for Downstream Bioprocessing

Chairs: Andrew Zydney and Michael Phillips

As the biopharmaceutical industry evolves, there is an ever increasing need for manufacturing solutions that offer increased productivity and improved economics without sacrificing process robustness. While there continue to be significant advances in downstream processing, truly "revolutionary" breakthrough solutions typically require the development of new materials with unique properties – membranes with novel retention or very low-fouling characteristics, chromatographic ligands with unique binding characteristics, materials designed to facilitate non-traditional unit operations (e.g., precipitation, flocculation, aqueous two-phase partitioning, etc.) that enable high selectivity, increased product throughput, and improved process economics.
This session will specifically focus on the development of new materials that have the potential to dramatically improve downstream processing. These developments include the use of "smart" (responsive) materials and technologies that provide enhanced purification, yield, throughput, product quality, process robustness, and/or process economics. Novel materials that integrate process monitoring and control (e.g., by detection of membrane fouling or product aggregates) will also be considered.

Questions to be addressed include:

- What are the current purification challenges within the biopharmaceutical industry that require the development of new materials/technologies?
- What new purification materials/technologies can offer compelling advantages to potentially change the paradigm of biomanufacturing?
- What are the unique advantages of these new materials?
- How can these materials/technologies be exploited to enable novel breakthrough solutions in the purification of high value biological products?
- What are the critical challenges that need to be addressed for the successful implementation of these new materials / technologies?

Session 5 – Tuesday morning, June 21

Purification - from Platform to Diversity

Chairs: Nihal Tuğcu and Dorothee Ambrosius

Cost pressure by payers and health care organizations are increasing and will drive innovation for novel biotherapeutics for unmet medical needs which are closely linked to and enabled by innovation in new production technologies. As a consequence biopharmaceutical companies must continuously improve and reinvent their development and production platforms to remain competitive and respond effectively to future challenges while balancing the potential benefits with regulatory constraints and technology risks. Despite the fact that mAbs are still the dominating molecule format allowing the successful application of purification platforms, the diversity in the biopharmaceutical research portfolio is increasing (including e.g., complex biologics with dual/triple targeting, conjugated mAbs, fragments, FABs, non –mAbs , "designer" molecules, new scaffolds) and driving the development of novel production technologies.

In this session, we would like to explore and discuss "smart" ways of bioprocessing to accommodate the diversity of molecule formats we are experiencing. Although platforms used for full-length mAbs may not be suitable, one might think how to utilize the benefits and knowledge gained across platforms over many years. With the help of HTPD, a quick optimization strategy to define the conditions for process steps, a "restoration" of the platform concept could be possible and would potentially lead to cost and resource savings. Another thought might be to increase the utilization of microbial expression systems for non-glycosylated products to drive cost down, but the advantages over a high titer short duration "CHO" system will need to be evaluated. Alternatively, it might be required to switch and move away from the existing platform processes to explore new affinity ligands or purification technology. In this session, we are looking for contributions that would help us define the "smart" bioprocessing for diversified pipelines:

- Could we stay with a platform approach while doing just the unavoidable optimization?
- What do we change most within the platforms to accommodate diversity?
- If we have to move away from platform, how important are HTPD methods and automation?
- Can we design smart novel formats addressing the innovation of biological function as well as exiting purification motive?
- Are there any potential affinity methods that could create robustness even in a non-Fc based purification process?
- How can we get to a point where the direct cost aspect of affinity chromatography no longer guides scientific rationale and value considerations take over?
- What are the key drivers and benefits to move to alternative technologies or expression platforms such as microbial?

Case studies and research towards guiding us through such questions are welcome and encouraged.

It may be Smart not to drift away into an alternative technology hype all too quickly just because we all enjoy change and challenges from new developments

Session 6 – Tuesday evening, June 21

Purification of non-protein products

Chairs: Caryn Heldt and Hari Pujar

The protein therapeutic industry has matured greatly over the last 30 years, and process solutions have kept pace with staggering improvements in productivity and costs over that period, rivaling previous accomplishments in traditional secondary metabolite pharmaceuticals. However, the non-protein biopharmaceutical arena, largely represented by vaccines, but also the burgeoning areas of cell, gene and nucleic acid therapies, provide unique process engineering and scientific challenges before the full potential of these modalities can be realized. In one case, vaccines have the unique requirement of needing to be produced at extremely low cost to ensure global use, but also burden the process to be extremely robust and rugged in order to be produced in parts of the world with developing maturity in the bioprocess ecosystem. On the other end of the spectrum, cell therapies, most prominently illustrated by the CAR-T approaches, challenge us to produce a personalized medicine that impose scale, time, and cost constraints unseen in other modalities.

Specifically the purification of these new modalities, in contrast to those for proteins and antibodies, provide unique purification opportunities and challenges. This stems from their distinct physicochemical make-up, which in turn results in sub-optimal performance when standard processing parameters are used. The classical example, discussed at previous Recovery Conferences, is of standard protein chromatography resins employed for these mostly larger entities. The bioprocess fraternity, with the rich experience of protein therapeutics, is poised to find fit-for-purpose ways of producing and purifying these products to enable an expanded toolbox to further broaden the frontiers of human and animal therapy. This session will explore the current bottlenecks and weaknesses in the bioprocessing of non-protein products and potential solutions to mature the industry.

- Is a platform process feasible for other new biologics and what would this look like?
- What are the real challenges of these molecules and how best to address these challenges?
- Does the development of affinity capture reagents make sense for these new non-mAb products?
- How does an efficient separation approach for a large vaccine product from its product related impurities look like?

Session 7 – Wednesday morning, June 22

Alternative Expression Systems: Strategic Impact for Biopharmaceuticals?

Chairs: Suzy Farid and Lars Pampel

CHO expression dominates our industry, with E. coli and yeast as noteworthy back-up options. This need not surprise: the performance of CHO systems is ever increasing, the scientific and technical infrastructure is established, and challenges remaining for this system are comfortably familiar to downstream scientists. Biopharmaceuticals today are an industry built on CHO**.**
And yet cellular and cell-free alternatives to CHO or *E. coli* expression have matured in recent years with the potential to offer superior yields, reduced impurity burden or better product homogeneity. This session wishes to debate if there is a need for such alternative expression systems for biopharmaceuticals, and how they would impact biopharma from a process development, manufacturing and commercial perspective. Do alternative expression systems offer sufficient attractive potential to enter the canon of biopharmaceutical manufacturing?

Questions to explore this arise from two different angles:

a) Developing a business case for alternative expression systems
- In view of the track record of CHO, is there any need at all for an alternative expression system?
- What gaps will alternative expression systems address?
- What is needed for these alternative production systems to "beat" CHO and *E. coli?*
- How do we change the equation away from CHO and the current dogma?

and

b) Changing the rules to achieve smart bioprocessing
- Given that the cell does the work of making our product – what will the expression system look like that voids the need for a 'Recovery' conference?
- Are cell-free systems feasible alternatives to cellular upstream systems? Will they radically simplify downstream processing?
- As downstream capabilities for dealing with impurities continue to increase, do host cell impurities still matter?

In keeping with Recovery tradition, we are looking for provocative contributions, featuring strong data and well-founded thought to feed controversial debate.

Session 8 – Wednesday morning, June 22

Biosimilars and Follow-on Biologics: Process Development, Similarity Assessment and Manufacturing Challenges

Chairs: Suresh Vunnum and Jill Myers

Biosimilars are biological medical products that are biosimilar to or interchangeable with a licensed reference product. The global sales forecast of Biosimilars in 2020 is $25 billion, and a large number of companies, both small and large, are developing Biosimilars of reference products. A myth is that Biosimilars development is easy compared to innovative pipeline programs. Although it is true that Biosimilars development does not entail identifying novel disease pathways, target validation or extensive clinical studies in all relevant indications, Biosimilars development is nevertheless quite challenging for the Process Development Scientist. Each biologic is unique and is characteristic of its manufacturing process. Several factors can therefore impact Biosimilars development, including use of different cell lines / unit operations / raw materials than that of the reference product, intellectual property restrictions, manufacturing supply chain strategy and process economic considerations. Each of these factors on its own, or an interplay between factors can influence the ability of the process to consistently deliver product quality attributes that meet analytical similarity expectations.

In this session, we look for views and answers on:

- What are the key considerations for Process & Analytical methods development for Biosimilars, including process control strategies used?
- How does upstream and downstream process integration impact Biosimilars development?
- What are the manufacturing and analytical similarity challenges with use of alternative cell lines and expression systems in Biosimilars development?
- What is the impact of scale and site changes on analytical similarity assessment (shown via case studies highlighting the issues and the mitigation strategies used)?
- What can we learn from case studies where intellectual property restrictions, regional requirements, economic considerations, manufacturing supply chain strategy presented a high hurdle for Biosimilars development?
- What can be said about the global regulatory expectations for establishing biosimilarity, as well as the approaches taken by various sponsors in establishing analytical similarity?
- How do developers go about establishing the analytical biosimilarity target space, including scope and extent of reference product testing?
- What recent high resolution analytical method(s) exist and how have these been leveraged to better understand ‘structure-function’ correlation?
- What are the statistical approaches used to establish analytical similarity criteria, including multivariate data analysis methods and technical considerations for establishing fingerprint-like similarity?
- How can one best establish "totality of evidence" for extrapolation and interchangeability of Biosimilars with originator products?

Session 9 – Thursday morning, June 23

Increasing Patient Access to Biopharmaceuticals – Cost of Goods is Only Part of the Story...

Chairs: Bruno Marques and Jonathan Coffman

Despite discussion at various forums, biopharmaceutical thought leaders have consistently ranked cost of manufacturing low in their priority list. One reason for that may be that the end-game for our industry should be maximizing patient access to biopharmaceuticals on a global scale. In this case, cost of goods is only a part of the solution, particularly due to the current disconnect between manufacturing cost and payer cost.
This session aims to explore technology development targeted at various cost scenarios, depending on expected market size for each asset. A fundamental quandary is how to balance patient access with profitability/sustainability of the biotech industry, especially in light of a competitive health care payer reimbursement environment worldwide.
In addition, we would like to put the entire cost of manufacturing and supply in perspective by exploring novel drug product technologies (e.g. spray-drying), as well as by taking into account product quality and regulatory constraints.

- What are the hot spots for costs in biopharmaceutical manufacturing and supply (including drug product manufacturing and analytical testing) and which of these could be entirely avoided or significantly reduced?
- What portion of the higher costs in biopharma is actually related to technology used and which portion of this technology is replaceable with much cheaper alternatives without a risk to quality?
- How much of a driver is there in any biopharma company to go down in cost below 1% of the selling price?
- Specifically, what are the best technical strategies to reduce DS manufacturing cost to $ 30-40/g (e.g. process intensification) and to $ 1-10/g (disruptive technologies for high dose/frequency assets)?
- Is disposable technology part of the problem or the solution?
- What does entire manufacturing process (cell line through filled vial) need to resemble in order to be routinely implemented in developing countries?
- How should our industry manage the regulatory and business risks associated with new technology implementation, e.g. chromatography resin cross-use, platform virus clearance data, vial fill in-place?

Session 10 – Thursday morning, June 23

Biomolecular Modeling for Manufacturability

Chairs: Chris Dowd and Peter Tessier

The ability to modify the properties of biological products to improve their manufacturability (e.g. reduced viscosity, aggregation and susceptibility to oxidation) requires a deep understanding at the molecular level. In addition, fundamental knowledge of a biological product at the molecular level is critical to rationally and efficiently design downstream and related processes. Smart bioprocessing means linking this fundamental biomolecular understanding to behavior in downstream processes, with the prospect of leveraging this knowledge to create more stable molecules and to shorten development timelines. Potential topics of interest for this session include: sequence screening strategies to identify hot spots, sequence/structural features leading to aggregation and mitigation strategies, QSPR correlations to batch or packed bed column behavior, 3D structure models for identification of surface features affecting chromatographic behavior and insights into mediators of high viscosity in protein solutions.

Questions to be addressed include:

- How can we best employ molecular-level understanding for bioprocess development?
- How can modeling be employed to determine which protein properties to modify to improve manufacturability and stability?
- How can we use molecular understanding to better predict process performance?
- What experimental and simulation tools are best suited for predicting and improving manufacturability?

Session 11 – Thursday afternoon, June 23

New Developments in Process Analytical Technologies (PAT) & Quality by Design (QbD)

Chairs: Gisela Ferreira and Thorsten Lemm

QbD (built in quality by design as a result of process and product understanding) and PAT (framework of technologies that provide timely measurement of variables known to affect product quality and are capable of controlling manufacturing processes) are two symbiotic and confluent concepts in biopharmaceutical industry that result in more consistent process performance, product quality and, potentially real time product release.
QbD is Smart when it increases process knowledge and enables consistent process performance and product quality outputs over many batches, campaigns, site transfers, and reduce quality oversight throughout the lifetime of the product. PAT is Smart when it can deliver simple process control to achieve more consistent process performance and product quality. It may also allow reduced user intervention to control the process and reduced quality testing.
Today, fourteen years after the release of the first draft of Pharmaceutical cGMPs for the 21st Century many QbD tools like risk based approaches and statistical process evaluations are widely used in the industry. However design space filings and PAT applications are still rare.

- Has QbD been successful to realize better returns on investment and improved the quality of the products by increased product and process understanding relatively to more traditional development approaches?
- Are there any case studies to illustrate enhanced process efficiency and/or flexibility on the production process activities as a result of using QbD and PAT in process development and manufacturing? Examples may include topics such as process monitoring, leaner manufacturing approaches and improved process and product control.
- How has QbD been supporting an easier, more fluid communication between industry and regulators? What have been the actual benefits to Industry? What is missing to fully realize the Regulatory relief suggested by the QbD paradigm?
- How are different Regulatory agencies (e.g. US, Europe and Japan) handling QbD based submissions and PAT approaches?
- QbD and PAT have been mostly connected with the main stream production process. How are these concepts being used to understand or facilitate raw material control, facility design trending and analytical development?
- Are there examples of novel approaches to PAT? What have been the development and trends? What is the vision for PAT?
- What is the impact and legacy of QbD and PAT on setting product specifications, process validation and continuous process verification?

This session invites papers that demonstrate the added value and discuss the current state-of-the-art of PAT and/or QbD in biopharmaceutical industry.

Session 12 - Thursday afternoon, June 23

Next Generation Unit Operations & Integrated Processes

Chairs: John Moscariello and Jeff Salm

Developments in product expression and the onset of new, but potentially unstable, modalities have sparked a renewed interest in operating cell culture continuously by employing perfusion. This session focuses on the integration or development of next generation harvest and downstream unit operations with a focus on handling product that is produced by the bioreactor in a continuous manner. In particular, this session will discuss unit operation integration, either through operating in a discrete, connected or continuous manner, as a means of "smart bioprocessing". These smart bioprocessing advances have the potential to drastically reduce facility footprints while maintaining throughput, enable low cost region-specific manufacturing to elevate regulatory hurdles, and/or significantly reduce cost of goods manufactured. Additionally, next generation unit operations may be needed to address these new obstacles. We are looking for a mixture of talks focusing on the development of enabling technologies and case studies or advances in process integration.

In particular, we are soliciting for abstracts that will spark debate around the following questions:

- What is continuous? What is integrated? What are the key drivers behind the current focus on integrated processing?
- Is a continuous or integrated process appropriate for all organizations? Where can it have the greatest impact?
- What are the gaps in current purification and harvest technologies to meeting the needs of a future next generation process?
- Do we have sufficient process controls and analytical tools to control CQAs in a continuous process?
- Is there an optimal approach to designing truly integrated processes?
- What emerging technologies and approaches will be our "Next Generation Unit Operations?"

Poster Session – Monday and Wednesday evening, June 20 and 22

Oceans of Innovation

Chairs: Abraham Lenhoff, Charles Haynes, and David Roush

Successful recovery of biological products requires a broad and diverse set of knowledge and approaches. We invite submissions related to the smart bioprocessing topics described for the oral sessions as well as those reporting innovative fundamental and technological advances, recent case studies that advance manufacturing knowledge, and fresh concepts that solve current or long-standing issues in downstream processing, including through exploitation of previously untapped knowledge from allied disciplines (e.g. blue sky approaches linking protein engineering and process development).

Debates Session – Tuesday afternoon, June 21

Chairs: Nigel Titchener Hooker and John Curling

The three debates will be featuring two opponents and one moderator each who will introduce and lead the discussion and get the involvement from the audience. In order to prepare the session and get a good match with the expectations of the audience the session chairs will call for questions to the opponents from RXVII participants well in advance of the conference. This will include a detailed description for each of the topics.

The three debates are NOT INCLUDED in the call for abstracts:

Debate #1 - "Design of Experiments (DoE) vs Modelling - show me the value"

Debaters: Karol Łącki and Jürgen Hubbuch
Moderator: Arne Staby

Debate #2 - "Disruptive technologies - why don't they stick?"

Debaters: Hanne Bak and Jörg Thömmes
Moderator: Todd Przybycien

Debate # 3 - "Continuous Processing - where should we be operating?"

Debaters: Konstantin Konstantinov and Brian Kelley
Moderator: John Curling

The debates will be run in series , so everyone can join each of the three discussions!