A Webinar Series

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Shaping the Future Pharmaceutical Manufacturing Landscape

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Collaborate to Innovate

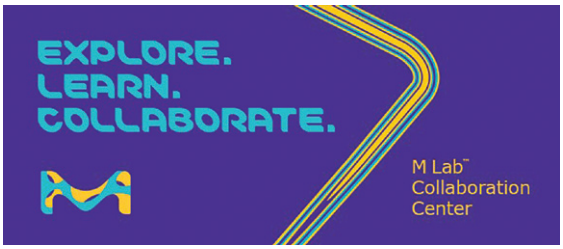
A Webinar Series

As the demand for new life-enhancing therapies increases globally, the pharmaceutical manufacturing community faces an unprecedented challenge to accelerate speed to market. Keeping up to date on industry trends is critical to maintaining a competitive edge. But how do you actively drive these trends and apply them to your manufacturing processes to bring your innovation strategy to life? Whether you are implementing single-use technologies to reduce costs and increase productivity or expanding your operations in emerging markets, scientific collaboration and access to global technical expertise are paramount in this dynamic environment.

We recognize that you need a partner who not only addresses today's challenges, but also anticipates future barriers that you may encounter while bringing your drug to market. This proactive mindset has driven us to establish our global network of M Lab™ Collaboration Centers. This network of facilities offers scientists and engineers a non-GMP environment where they can examine unit operations along their bioprocesses to optimize, analyze, and troubleshoot in real scale without the strict requirements of their own production facilities. From São Paulo to Seoul, our network of technical experts harness the power of collaboration to help you think big, think outside the box, and improve your biomanufacturing process.

In a recent three-part webinar series hosted by *BioProcess International,* three experts representing our M Lab™ Collaboration Centers shared their perspectives on the future of the industry and provided specific case examples that demonstrated how collaboration enables improvements that are shaping the future pharmaceutical manufacturing landscape. From collaborative efforts in next-generation bioprocessing to partnerships that opened doors in emerging markets, the speakers covered strategies for managing risk, expanding geographic footprint, and staying ahead of the competition:

• Understanding future pharmaceutical industry trends and how to address them with your manufacturing process



• Trends and drivers leading to an emerging paradigm shift toward continuous bioprocessing and how an EU-funded industry collaboration successfully developed a new next-generation downstream platform

• Strategies for applying single-use technologies and next-generation processing to address production needs in emerging markets while reducing risk, capital investment, and timelines.

Each 10-minute presentation was followed by a Q&A session, and summaries are included in this *BioProcess International* insert. The full, on-demand versions of these webinars are available online: www.bioprocessintl.com/ask-the-experts/collaboration-to-innovate-webinar-series.

With novel approaches to patient treatment on the horizon, it is an exciting time to be a part of this industry. Although this webinar series touches on just a few of the many outcomes of scientific collaboration, we hope that these success stories are a source of inspiration. When we truly come together as a global scientific community, we can solve the toughest development and production challenges.

—Dr. Andrew Bulpin
Executive Vice President
Head of Process Solutions
MilliporeSigma

Explore, Learn, Collaborate

Enabling Future Trends in Biomanufacturing

with Dr. Helge Berg

On Wednesday, 26 April 2017, Dr. Helge Berg (head of global customer experience and education at MilliporeSigma) presented a BPI "Ask the Expert" webinar. He discussed how pharmaceutical manufacturers, vendors, and regulators should explore new avenues, learn and share expertise, and collaborate with one another to move successfully into the future.

Berg's Presentation

Exploring, learning, and collaborating should touch all levels of the "Supplier Hierarchy Pyramid" (adapted from Roche/Genentech): starting with the foundation of assuring material supplies (for manufacturers and patients) and proceeding up through quality/regulatory compliance, service, and cost of ownership to innovation.

Mature markets are striving toward optimizing and intensifying processes (e.g., through fully continuous, disposable processes) to lower cost and save time. There also is a drive toward novel modalities: new molecular entities, gene therapies, viral vectors, and biosimilars. In emerging markets, we see a prevalence of classic pharmaceutical processes producing vaccines, plasma-fractionation products, small molecules, and eventually biosimilars.

Along with their product portfolios, vendors should offer an abundance of technical and application expertise linked with appropriate technical infrastructure. MilliporeSigma provides nine M Lab™ Collaboration Centers, seven of which are located in emerging markets. These are globally networked facilities where customers can explore technologies, get training, and work together with us to develop new technologies and manufacturing approaches.

About 10 years ago, Singapore decided to implement large-scale bioprocessing. The government engaged vendors and academic partners to ensure that it could attract, develop, and sustain a highly skilled and resilient workforce for biomanufacturing. Our company has been a key partner in that goal. To date, we have trained 70% of the Singapore pharmaceutical workforce, 80% of whom are employed today in manufacturing operations. We also train regulators. In the past few years, we trained dozens of Chinese FDA inspectors to help them understand and stay current with global regulations.

In a Horizon 2020 collaboration funded by the European Commission, we are closely working with industry partner Sandoz (Novartis) and multiple academic partners in developing next-generation processing approaches. Our industry overall has a goal of making processes more efficient and economical, including moving toward fully disposable, continuous processing. We are using existing technologies in new ways and developing new technologies for intensified and linked processing.

Questions and Answers

In what emerging areas do you expect the most dynamic growth? I see countries such as Taiwan, Indonesia, the Philippines, and Malaysia investing significant efforts and money into their pharmaceutical and biopharmaceutical manufacturing. Brazil and Mexico in Latin America also are on a steep growth path. Africa is establishing manufacturing for vaccines.

Can you give some examples of process intensification? In-line, single-pass tangential-flow filtration (TFF) helps to concentrate feed streams to enhance chromatography performance, for example, or enhance ultrafiltration performance. It allows you to concentrate volumes significantly, debottlenecking processes and reducing tank volumes. Other approaches include continuous processing. Some operations (e.g., viral filtration) traditionally have been validated as batch processes. We've presented to regulators ways to allow for in-line virus spiking that mimics actual continuous-process conditions for validation. Also, the use of activated carbon in certain applications is an old technology with great capacity and capabilities.

What are the M Lab™ Collaboration Centers? They are GMP-like technical facilities where clients can test our non-GMP equipment and technologies in real-life applications. They can work with the systems and get trained on them while working side-by-side with our technical experts. It's a collaborative space where we foster open communication. We have one lab each in North America, Europe, Brazil, Singapore, Japan, South Korea, and China, and two in India. I am very sure we will open more in the future.

A Case Study Industry Collaboration Makes Next-Generation Biopharmaceutical Processing a Reality

with Ms. Merrilee Whitney

In a BPI "Ask the Expert" webinar on Wednesday, 31 May 2017, Ms. Merrilee Whitney (head of next-generation monoclonal processing at MilliporeSigma) discussed the Horizon 2020 program, showing how collaboration can forward and advance technologies associated with next-generation processing.

Whitney's Presentation

Many definitions of *next-generation* exist within the industry, covering cover process compressions, brand new facilities leveraging single-use technologies, and fully continuous and connected processing. So it is important to understand the drivers and trends pushing their adoption.

Trends are toward smaller annual production needs, improved process efficiencies, and increased focus on product quality. Companies are looking for flexibility in their manufacturing networks. They see an increased level of process complexity. Driving the new technologies are increasing downstream process bottlenecks, facility-fit limitations, and desires to increase speed to clinic and reduce cost of goods.

Three key areas are critical to implementation of next-generation technologies: process intensification, implementation of single-use technologies, and associated process analytics. Ultimately, this will evolve into a fully connected, fully continuous process.

Regarding customer collaborations, we have an example in the Horizon 2020 program. Announced in 2014, this is the biggest EU research and innovation program ever funded and is divided into three parts: excellent science, industrial leadership, and tackling societal challenges. One project is led by Lek Pharmaceuticals in Slovenia and includes MilliporeSigma in France, Sandoz in Austria, and other industry and academic participants with the ultimate goal of implementing a fully connected and continuous process. Focus areas include upstream use of flocculants and TFF, continuous capture, single-use technologies, and advanced analytical tools. Our consortium will evaluate and select the best-in-class technologies for each area while considering implementation hurdles, economics, and environmental impact. For example, we found that we can use a continuous multicolumn chromatography operation with multiple steps in parallel to get up to 90% higher resin use.

Biomanufacturers are moving toward a fully continuous process based on single-use technologies. This future achievement will be an evolution starting with upstream and downstream process intensification, beginning to connect some of those intensified processes, and then arriving at a fully connected and continuous process. Collaborations are critical to meeting the challenges associated with next-generation processing, from the molecules to the applications to the process analytics, with perspectives from both customers and suppliers, to bring together the entire picture.

Questions and Answers

How does MilliporeSigma manage collaborations with customers? We have a rigorous process of establishing a dedicated project team and project manager. Working with a customer, we define the scope and mutual goals. Regular meetings are set-up, along with a detailed project plan including key milestones.

Is MilliporeSigma collaborating with customers to help develop other technologies? Yes, we are looking to establish collaborations and develop our next-generation portfolio with our core businesses (filtration and chromatography) as well as cell culture media, single-use and multiuse systems, and consumables.

How do you see the adoption of next-generation process technologies evolving? It will depend on the type of customer: e.g., established or emerging company, improving an existing facility's efficiency or looking to expand. I see this as a step-wise progression toward fully connected and continuous processes.

How have you seen next-generation technologies help customers? One example was an increase in cell density and titer after using perfusion in an upstream application. It improved manufacturing capacity and drove a >50% reduction in capacity use. We've also seen cost-of-goods reductions >75% from lowering buffers, water, and chemical use and chromatography resin costs. Increasing the number of manufacturing runs per year with greater efficiency also will improve processing time and decrease labor.

Emerging Pharmaceutical Markets

How Collaboration Fosters Growth and Minimizes Risk

with Dr. Bala Raghunath

Bala Raghunath (director of global manufacturing sciences and technology for MilliporeSigma) is the company's leading expert on biopharmaceutical purification processes. In a BPI "Ask the Expert" webinar on Wednesday, 28 June 2017, he shared considerations that companies should factor into their plans to manage risk while expanding into emerging markets.

Raghunath's Presentation

Emerging markets face a number of common challenges and needs: e.g., speed to market, accessibility to technical and application expertise, attracting and developing local talent and workforce skills, navigating an uncertain and evolving regulatory environment, and developing an appropriate manufacturing infrastructure. Overall, this presents a need for a comprehensive end-to-end solution and creates a tremendous opportunity to collaborate with trusted supplier partners that can offer global networks, technical infrastructure, capabilities, and experience.

Such collaborations can nurture growth by helping companies address developmental scaling and operational challenges. They can reduce development timelines through a holistic approach to process optimization. That is enabled by a vendor's comprehensive knowledge base, diverse experience, and strong global network. For example, know-how relating to applications, products, equipment, and operating methodologies may be applicable toward a number of biomanufacturing processes. Some suppliers have collaboration laboratories designed to cater to end-users' developmental needs. Such capabilities help to reduce start-up delays and ensure predictable, scalable, and reliable operations.

Case Studies: An emerging-market customer faced significant challenges in achieving desired levels of feed and purity for a fusion protein expressed by Chinese hamster ovary (CHO) host cells. Very high impurity and aggregate levels (~10%) required a very robust process with high yield and purity. And of course, the timelines were tight. We collaborated with this customer to screen several different resins and operating conditions with a high-throughput method in our local M Lab™ Collaboration Center laboratory to optimize the process. The project took about four months, but in the end we established a robust purification process that met both purity stipulations, and we successfully transferred that process to manufacturing.

Another case involved a single-use final fill–finish operation. An emerging-market customer wanted to establish a single-use final step for a cytotoxic drug filling application. A set-up in our local M Lab™ pilot facility established and demonstrated the required operations for successful filling. Those sequences were further fine-tuned during a visit by the customer to our laboratory, so the design was finalized with customer input. In the end, we established a process for single-use mixing and final sterile filtration of final bulk drug.

We also put together a training program in collaboration with the Singapore government for its Workforce Development Agency (WDA) through a consortium of companies that had moved to set-up manufacturing capabilities in the area. The objective was to attract, develop, and sustain a highly skilled and resilient workforce for the biomanufacturing industry. As a key part of this consortium, we developed several operator and supervisory training programs and delivered top skills to the local workforce. At the most recent count, roughly ~70% of the Singapore pharmaceutical workforce was trained by our company, and ~80% of those people are serving in manufacturing operations.

Questions and Answers

Do you mostly offer standard training courses, or would you be willing to provide custom courses? We offer both. Typically we discuss with an end user to determine its specific training needs.

What is the best way to determine the regulatory requirements in different emerging markets? More developed emerging markets (e.g., China, India) have their own health authorities, so the best way is to reach out and seek out an audience with them. Over the past decade, they have found the need to establish local regulations and created their own regulatory guidelines specifically applicable to their markets.

You can also seek out experienced supplier companies. Many have good knowledge about how things get done in other markets. You may use that as a lead-in toward discussions with regulators in a given market.

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