Biopharmaceutical Training

Train Your Team to Meet Evolving Industry Needs

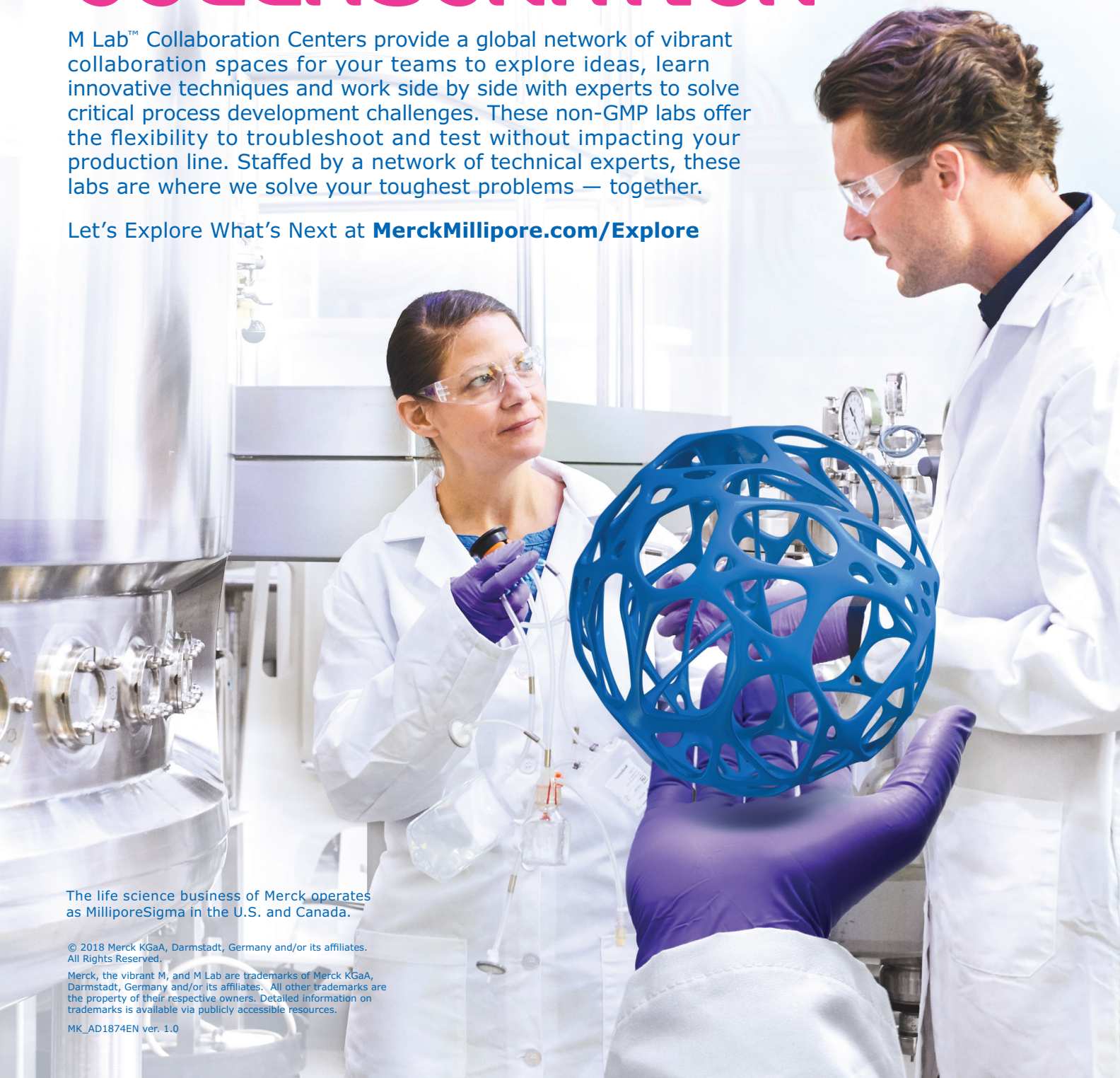
BioProcess™ INTERNATIONAL
eBOOK Series 2018

M Lab™ Collaboration Centers

EXPLORE COLLABORATION

M Lab™ Collaboration Centers provide a global network of vibrant collaboration spaces for your teams to explore ideas, learn innovative techniques and work side by side with experts to solve critical process development challenges. These non-GMP labs offer the flexibility to troubleshoot and test without impacting your production line. Staffed by a network of technical experts, these labs are where we solve your toughest problems — together.

Let's Explore What's Next at **MerckMillipore.com/Explore**



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From the Editor

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Welcome to this year's focus on industry training programs. In the past three years we've brought this information to you in several forms: as a full supplement issue (2016), a featured report (2017) — and now this ebook. Each program that we've profiled offers its unique approach to training present and future biotechnologists. The best of the programs offer hands-on training with current equipment provided by supplier partners and with up-to-date approaches to documentation and regulatory requirements. Many university- and community-college–based programs, once lacking in practical, GMP training, now also benefit from a wealth of hands-on manufacturing experience toward resolving real-world issues.

So far, beginning in late 2016, BPI has profiled the following training programs:

- the Biomanufacturing Training and Education Center (BTEC), North Carolina State University (and related NCSU course offerings)
- the UCL Department of Biochemical Engineering's Modular Training for the Bioprocess Industry (MBI) program
- the Biotech Training Facility, Leiden Bioscience Park, the Netherlands
- the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL)
- the International Society of Automation (ISA), the Automation Group, and the American Society of Engineering (example programs that focus on automation and related requirements)
- the National Center for Therapeutics Manufacturing, Texas A&M University
- the Singapore Institute of Technology
- Solano and Miracosta junior colleges (CA)
- company/supplier-sponsored courses, including those offered by Biogen, Fujifilm DioSynth Biotechnologies, Novo Nordisk, Sartorius, and in this ebook, Merck.

This ebook continues to help us explore the theme by offering an example of how a major industry supplier conducts training with its equipment and supported processes. The second article profiles a training program within BPI's own, larger company (Informa) that develops courses in collaboration with industry consultants.

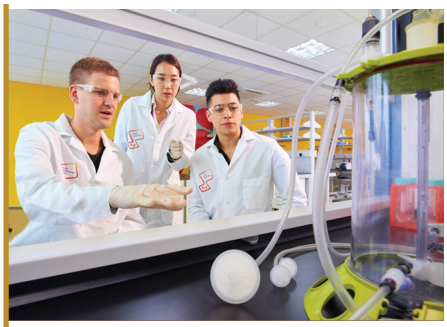
What Do You Think?

BPI is committed to letting its readers know about as many courses and training options as possible. But to do that, we need to hear from you. Have you attended a course that you found particularly useful? Has an outside training program brought a course into your company that was uniquely relevant to your work? What can you recommend, and why? Where are the so-far hidden gems of instruction specific to instrumentation, processes, and project management? And where have you noticed gaps in available course offerings — information that could help guide a group toward developing a new course or program? Send me your recommendations, and help us plan for our focus on training in 2019.

Time to Get Hands-On with Upstream Technologies

Train Your Team to Meet Evolving Industry Needs

Delia Lyons and Herb Lutz



Choosing a knowledgeable training partner is an important step for pharmaceutical companies to take in order to address gaps in technical expertise.

An estimated 50% of the pharmaceutical industry's new product pipeline comprises biological products, a drug class that accounts for an increasing proportion of FDA approvals each year. Because the design, construction, and validation of biologics manufacturing plants take years to finalize, pharmaceutical and contract manufacturers around the world are investing rapidly in new facilities to accommodate projected demand. In the race to increase capacity, such companies must optimize their approaches to facility design and process development. Biomanufacturers are driven by the common goals of minimizing capital investment and product cost, mitigating risk, and hastening new products through clinical development to benefit patients as quickly as possible.

New Challenges and Demands for Continuing Education

Fed-batch processing has been a mainstay in the industry. However, newer techniques can increase the efficiency of both clinical and commercial production operations. The rapid expansion of bioprocessing capacity around the world, combined with emerging technologies, has resulted in a hiring surge — and a growing need to train new employees on the latest technologies in upstream cell culture, including perfusion and intensified upstream processes for manufacturing biological products.

An enhanced understanding of newer processing methods can be extremely helpful for both new hires and experienced bioprocessing professionals. The need for training in upstream processes has become particularly acute at companies in emerging markets and at those needing to adopt next-generation technologies to facilitate the transition from traditional fed-batch systems to continuous upstream processing.

Although upstream technologies are critical to upstream process specialists, training courses also may interest downstream processing specialists who want to learn more about upstream operations. Seamless integration of upstream and downstream components of bioprocessing is a growing industry need. The movement toward greater integration is bringing to light some of the purification challenges that can arise during both upstream and downstream processing. This new awareness prompts many companies to explore how to streamline the overall manufacturing process to reduce costs and increase efficiency. In this context, financial and managerial professionals can benefit by learning about the latest manufacturing processes and challenges and, as part of strategy, operational and financial goal-setting.

Whereas some larger biopharmaceutical companies and contract manufacturing organizations offer such training in-house, other companies choose to send their employees to external training programs.

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Reasons to subcontract training include a lack of resources, in-house expertise, or facilities and the wish to expose employees to more diversified technologies, approaches, and perspectives. When evaluating bioprocessing training programs, companies should seek out a few key features to ensure that the knowledge trainees bring back can be put to work in real-world environments and yield desired intellectual, operational, safety, quality, and financial benefits.

Focus on Perfusion and Process Intensification

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The intensification of perfusion presents new technological challenges and the requirement for a new set of technical skills and knowledge. A high-quality upstream cell culture course ideally should include a lecture portion on the basics and theory of perfusion, which is not itself a new technique, but which recent technological developments have made newly relevant, especially in biologics manufacturing.

For example, biopharmaceutical professionals increasingly are interested in adopting **process intensification,** a method closely related to perfusion. Instead of growing cells in a traditional seed train and transferring them to a sequence of larger vessels to achieve enough biomass, intensification enables a reduced stepwise scale-up to production levels by using a production-scale perfusion bioreactor that incorporates advanced growth media. Process intensification can accelerate upstream processing and thereby shrink development time lines and increase productivity.

Understanding intensified, perfusion-based processes is increasingly relevant as market dynamics continue to change. In this era of expanding globalization, many multinational companies are contemplating more distributed manufacturing models by establishing smaller facilities in widely dispersed geographic areas rather than manufacturing in a single, large plant. The cost- and time-saving benefits resulting from process intensification provide a competitive price advantage that ultimately enables manufacturing of orphan drugs, potentially in portable plants. Furthermore, some companies also are exploring the use of intensified perfusion for the creation of biosimilars and biogenerics.

Learn from the Experts at the M Lab™ Collaboration Centers

At Merck, the M Lab™ Collaboration Center in Burlington, Massachusetts, USA, is part of a global network of nine non-GMP facilities designed to spark scientific curiosity and problem-solving in a collaborative environment. As an integral part of the company's expansive training curriculum, the site enhances opportunities to work with customers and demonstrate new technologies. The laboratory also provides space to simulate large-scale commercial operations and focus on industry issues — and ways to address them.

Merck recently created a new training course, "Continuous and Intensified Processing in Upstream Cell Culture," to provide a sound foundational understanding of new upstream processing techniques. The three-day course was inspired by customers clamoring for enhanced educational opportunities on the latest technologies. The course will be launched in the United States, with future sessions at M Lab™ Collaboration Center locations in Europe and Asia, customized to meet the needs of those specific markets.

Attendees will build understanding of

- Perfusion systems and their potential applications
- Recombinant cell lines, including transfection processes, and methods and criteria used for screening and selection of recombinant cell lines
- Cell retention devices
- Cell culture media, media optimization, and selection criteria; the differences between fed-batch and perfusion small-scale models and hydration methods
- Assessment techniques for growth media filter sizing and selection for various formulations and scales
- Bioreactor components, controls and scalability, as well as basic operation of a perfusion system using a filtration-based cell retention device.

Course Components — Lecture and Lab

Lectures provide an overview of basic concepts in continuous and intensified upstream processing and describe the primary differences between traditional and intensified processes. Laboratory work provides practical experience toward applying some of the new methods to address common industry pain points in three key areas.

Cell-Line Development, Transfection, and Cell Metabolism: Students will learn and practice common methods used for cell-line engineering and development, along with considerations for critical Go/No-Go decision points and discussion of troubleshooting for common issues and technical difficulties.

Cell Culture Media: Students learn about critical components of cell culture media, methods of optimization, principles of hydration, mixing, and filter sizing.

Bioreactors and Perfusion Devices and Assemblies: Students take samples from bioreactors, study metabolites, interpret data, recognize warning signs, and troubleshoot problems. Participants also experience real-world conditions and build problem-solving skills.

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Merck Training Resources

Learn more about Merck's training program at www.merckmillipore.com/training

Learn more about the M Lab™ Collaboration Centers at www.merckmillipore.com/mlabs.

Instructor Qualifications

Companies evaluating training alternatives should verify that instructors have extensive industrial expertise in the subject matter. Course instructors should have specialized expertise in cell-line engineering and development, perfusion media development, bioreactor process development, bioreactor scaling-up, and approaches to troubleshooting.

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Providing the Right Tools for Success

When evaluating a training opportunity, biopharmaceutical professionals should scrutinize the course curriculum to ensure that it provides the right tools for students to gain understanding and competence in applying and troubleshooting new bioprocessing technologies, equipment, and techniques.

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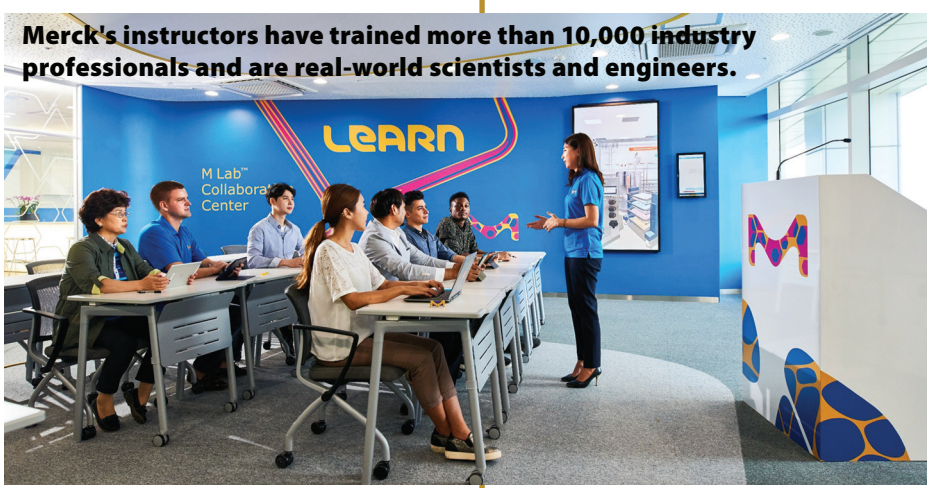
Course Checklist:

- Holistic approach to the entire upstream process
- Focus on perfusion and process intensification techniques
- Qualified staff with real-world industry experience
- Integrated classroom training and hands-on simulations.



Merck's instructors have trained more than 10,000 industry professionals and are real-world scientists and engineers.

Delia Lyons *is head of perfusion media development, and* ***Herb Lutz*** *is global principal consultant, manufacturing sciences and technology, at Merck; delia.lyons@sial.com; herb.lutz@emdmillipore.com.*

Pharmaceutical Training International (PTI)

Interactive Training for Life-Science Professionals

Roisin Manning and Susannah Campbell

Pharmaceutical Training International (PTI) was founded in 1992 to provide interactive training to aspiring life science professionals. With a developing portfolio of biopharmaceutical courses, PTI offers industry-leading training from its faculty of expert trainers, each with at least 10 years of relevant industry experience. PTI offers a range of learning experiences, with online, face-to-face, and customized options. Recent attendees have included colleagues from companies such as Johnson & Johnson, Merck Serono, and Janssen.

Immersive, Supportive Learning Environments

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PTI offers a comfortable learning experience at luxury hotels in London and other European capitals for its public training courses. The courses are designed to accommodate small groups to create an interactive environment where all can benefit from a trainer's wealth of knowledge. This environment also provides attendees with the opportunity to network and learn from one another's experiences as well as expand their collaborative pool of knowledge through group exercises and case studies in friendly and informal settings. The typical format of two days of intensive learning allows attendees to spend limited time away from the office and learn in an immersive and supportive atmosphere.

Staying Relevant: PTI courses are developed in consultation with industry to gain a comprehensive understanding of what content is most relevant for the current market. The goal is to produce the most up-to-date content and to include innovative ideas for courses responding to industry needs. Furthermore, PTI welcomes feedback from attendees of its courses, both to improve the running courses and ensure a high standard of teaching and to aid in research and production of new content.

Example course: Introductory Level CMC Analytical, Comparability, and Stability Testing and Lab Practices for Biotechnology and Biosimilar Products

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Trainer Nadine Ritter presents a concise but inclusive overview of all relevant regulatory, technical, and quality elements necessary to assure successful design, implementation, and documentation of required CMC analytical and stability studies for biotechnology products, including biosimilar products. Attendees are given a USB drive containing a complete set of all regulatory documents and industry white papers that are currently applicable to biopharmaceutical analytical

CMC requirements. Up-to-date CMC analytical and stability issues are explored, and strategies for addressing missing information are discussed.

Interview with Nadine Ritter: At the running of her courses in London in June 2018, PTI interviewed Nadine about the value her courses hold for industry.

PTI: Why do you think your courses are so long-running and popular?

Ritter: Speaking first to the introductory level course; over the years, I have taught multiple generations of colleagues from the same company — people learn about the classes by word of mouth. The way that the courses are structured allows delegates to gain a common view of current challenges. I update the course materials all the time, given the constantly evolving nature of our industry, but no matter when they attend, the course is a great opportunity for students to spend two days and immediately come up to speed on the subject matter. In addition, we explore what studies you must do during development that are analytical driven. I use practical examples from my own experiences and observations so people can compare to their own strategies. I see so many "A-ha moments" on this course as people put things in context!

In addition, I give attendees an analytical resource package to take away with them — all the up-to-date regulatory documents and publicly available white papers and FDA warning letters. All my slides are referenced, so you can look up the original document later and review. I'm a big believer in being able to make a knowledgeable decision, for which you must know where the requirements are written and what the core concepts mean. The introductory level course provides this useful snapshot.

PTI: And why do you think the advanced level course has proved valuable?

Ritter: The advanced level course allows us to go into details. For example, what is a reference standard protocol and what would go in it? How do you perform comparability studies? What do you do for validation of stability indicating methods? The advanced class is more focused on the how, not the what. The two courses allow us to cover the whole spectrum. They set everyone up for the same terminology, the same view and understanding, in a way that's very useful for delegates to bring back to their organizations — which is why I see so many attendees who have been referred to this course by their colleagues. There is so much information out there, it is challenging to know what's relevant and what's official. What industry organizations are well respected and what publications and white papers can be relied on? What should you be taking advantage of? It's important to become engaged with the resources available, and these courses are a great way to start and continue that.

PTI: Do you think getting to grips with this wealth of guidance and documentation presents a challenge for industry?

Ritter: When I first came into the industry, there were no training classes like mine and very few other resources. There was no internet, and I had to learn in parallel to the industry developing. Now, of course, there's much more information, and we have an opportunity to review what we know so far. If everyone hears the same message and gets the

Dr Nadine Ritter *(analytical advisor with Global Biotech Experts LLC) is a renowned world authority in providing guidance and practical training in CMC analytical elements of biotechnology/biosimilars and laboratory quality practices. She is the trainer for PTI's courses Introductory Level CMC Analytical, Comparability and Stability Testing and Lab Practices for Biotechnology and Biosimilar Products and Advanced Level CMC Analytical, Comparability and Stability Testing and Lab Practices for Biotechnology and Biosimilar Products. Ritter also is a long-time member of BPI magazine's editorial advisory board.*

same level of background, I think it accelerates discussions and reduces miscommunication.

PTI: How do you keep yourself up to date in such a constantly-evolving sphere?

Ritter: I'm in the field as a consultant most of the time. Training is a real passion, but if I didn't consult as well, I would immediately become irrelevant. If I'm not actively engaged in this work, I would have no new material to bring back. Just this week, new warning letters have come out that are relevant, and there's a new FDA guidance document. It's important to incorporate developments into the class. To do this, I use my other activities to inform the training and provide richer practical contexts. The minute I stop being engaged and actively doing this work, I won't be an effective trainer. PTI does not have full-time trainers, but consultants who bring their current experiences and are able not only to explain concepts, but show how they apply and their real impact on our industry.

Delegate Case Studies

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Emma Maloney (site regulatory manager, Fujifilm Diosynth Biotechnologies) attended Introductory Level CMC Analytical, Comparability and Stability Testing and Lab Practices for Biotechnology and Biosimilar Products in June 2018.

As a site regulatory manager, I'm responsible for our own regulatory obligations for the United Kingdom. We are a contract development and manufacturing organization (CDMO), so I also assist and consult with customers on their regulatory journeys. I chose this course because my background is biochemical engineering — I'm a chartered engineer. I moved into regulatory affairs about seven years ago. My home territory is process engineering and the process side of these products, and although I have learned a lot about analytical testing from colleagues, I felt I needed an analytical course that formally taught some of those aspects. The process and the analytical side both have to marry for a submission to be successful. The title of the course, which specified biotech and biologics, was really encouraging for me. Historically, there wasn't as much training aimed at these kinds of products as for small molecules, but now more and more is becoming available.

I chose PTI because I have attended courses in the past and know and trust the brand. PTI released a free webinar with Nadine last year, which I found very valuable. I then decided that I had to attend her course. I have found the course to be very useful in helping filling in some gaps and bringing me more up to date. This is a fast-changing field, and guidances evolve all the time. It's essential to focus your finite resources on the best approach and what the regulators are looking for. Going forward, I want to work closely with my counterpart in the United States to ensure we are giving coherent guidance to colleagues and clients. It's important to attend courses like this and share new information when I return to work because the knowledge I gain becomes embedded into the offerings we give our clients over time.

Derek Bothby (analytical specialist, Ipsen Biopharmaceutical Ltd.) attended Advanced Level CMC Analytical, Comparability and Stability Testing and Lab Practices for Biotechnology and Biosimilar Products in June 2018.

I chose this course because it seemed relevant for my company's current situation. We have new products in their early phases, and I wanted to build my knowledge on what is required from an analytical viewpoint for each clinical phase on the way to final submission. My own background is laboratory based, and I am now running stability studies for new products to support clinical and preclinical studies. I wanted to build on my regulatory knowledge and have found this course useful in building up my understanding. I have found it beneficial that the course covers both US and European regulations and clarifies where the crossovers are. Nadine presents very well and provides a lot of background — and in a way that will enable me to apply this in my day-to-day role. I would most definitely return to a PTI course in the future.

Roisin Manning *is senior product manager and* ***Susannah Campbell*** *is a junior producer for PTI. For further information on these or other PTI courses, contact* ***Nabihah Durrani,*** *Nabihah.Durrani@knect365.com.*

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