# Facilitating Workforce Development

A case study on improving single-use training through vendor and end-user collaboration


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SPECIAL REPORT

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## A Case Study on Improving Single-Use Training Through Vendor and End-User Collaboration

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Collaboration between end users and suppliers on single-use technologies (SUTs) has increased tremendously in the past few years, particularly through the efforts of industry groups such as the BioProcess System Alliance (BPSA) and BioPhorum. Both have fostered working environments in which to share ideas substantially, focusing largely on technological aspects of SUT design and implementation. Training, however, could benefit significantly from collaborative efforts between SUT suppliers and end users. Despite vendors' extensive efforts to ensure the integrity of single-use systems and components during their assembly and packaging, damage leading to leakage can occur throughout the SUT life cycle, especially when bioprocess containers are handled improperly during shipment, interim storage, unpacking, installation, and ultimately operation (Figure 1) (**1**).

To meet current good manufacturing practice (CGMP) requirements and ensure process quality, SUT operators must have high-quality training in handling, installing, and operating single-use production systems. Yet it has become increasingly difficult to provide such instruction. SUT adoption continues to grow as the biopharmaceutical market expands, and as many COVID-19 vaccines and other novel medicines move through phase 3 clinical trials to market approval, demand for well-trained SUT operators is growing faster than existing training infrastructures and methods can cope with.

Gaps in employee and contractor training remain a top reason why drug manufacturers fail CGMP compliance inspections by regulatory authorities (**2**). Unfortunately, operator error causes more batch failures at the commercial stage (4.3%) than it does at clinical scales (3.5%) (**3**).

Potential for single-use biocontainer breakage — due to shipping or handling errors — is a top reason that biomanufacturers have not implemented SUTs more widely than they have (Figure 2) (**3**). BioPhorum reports that leakage can cost anywhere from US$50,000 to >$20 million depending on the type of bag and the material it contains (**4**).

BioPhorum also notes, however, that improved training methods could considerably decrease the occurrence of leakage. The group has developed a

**Figure 1:** Single-use technology life cycle at an end-user facility

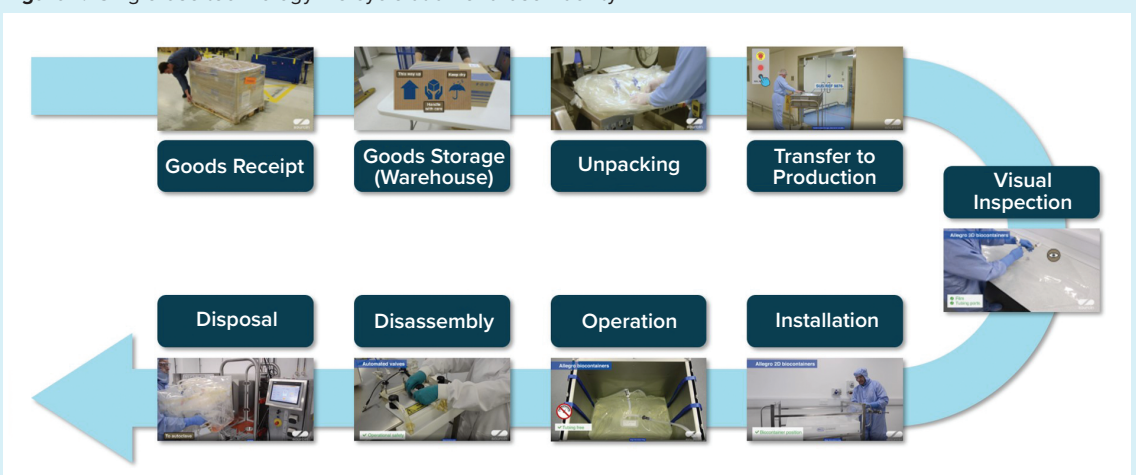


**Figure 2:** The top three reasons preventing further implementation of single-use technology (SUT) in biopharmaceutical operations, as reported by drug developers and contract manufacturing organizations (CMOs) in the BioPlan Associates *18th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production* (**3**)

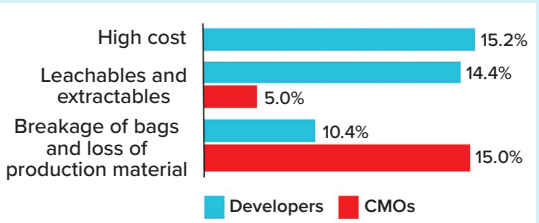
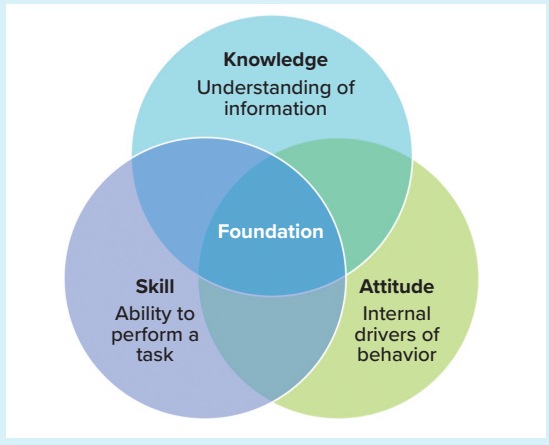



**Figure 3:** Training for competence requires a combination of knowledge acquisition, practice of skills, and behavioral change to ensure that operators follow the same procedures every time.




toolkit for training operators to handle single-use assemblies and components in ways that minimize user error (**4**). SUT implementation requires a different skill set than that needed for traditional stainless-steel equipment: Operators must be trained on the unpacking, visual inspection, installation, inflation/leak testing, sterile connection, disconnection/disassembly, and disposal of contact items to prevent system/component damage and to minimize contaminations that can cause manufacturing failures.

## Addressing the SUT Training Gap

Through discussions at biopharmaceutical industry conferences, Pall and Lonza recognized a mutual desire to improve SUT training and reap the obvious benefits of working together to develop fit-for-purpose solutions. Lonza offered to share current operational experiences and help evaluate new training tools and platforms during the development process.

The companies began collaborating under a confidentiality agreement, with frequent meetings to ensure consistent, ongoing communication. Development of effective SUT training modules required transparency about the partnership's goals and extensive sharing of experiences about what handling strategies do and do not work on the facility floor. Information sharing also was critical to supporting improvements in SUT design.

The companies have since identified projects for which there is a clear need for improved training and from which mutual benefits can be drawn for training solutions and new SUT design elements for simplified handling. The focus largely has been on achievable targets for which results can be observed quickly. In addition, both companies have evaluated their respective training programs to create benchmarks and identify capabilities and resources.

Subsequently, Lonza's understanding of training fundamentals, adult learning styles, and operational constraints were aligned with Pall's knowledge of SUT equipment, handling, and operations to develop a novel training approach leveraging state-of-the-art digital tools, virtual reality (VR) solutions, and interactive in-person sessions.

## Understanding SUT Training Needs

Developing an SUT training program required understanding of adult learning and of optimal strategies for teaching operators about SUTs. Such programs need to be easily scalable across companies of different sizes, and they should leverage the best learning and teaching methodologies while accommodating the physical constraints of some single-use equipment. Information should be accessible and applicable regardless of skill level, especially considering the increasing number of employees who enter biopharmaceutical manufacturing with limited or no practical experience — and COVID-related reductions in hands-on modules for bachelor- and master-level courses.

Studies have shown that most adults prefer to learn by doing and retain more knowledge when participating in the learning process, such as in group discussions, practicing, and teaching others (**5**). A blend of face-to-face instruction, e-learning in virtual classrooms, and VR/mixed-reality (MR) training was determined to be the best approach.

Training activities must achieve rapid, scalable SUT knowledge transfer to ensure that the biomanufacturing workforce can perform CGMP-compliant, aseptic, single-use bioprocesses reliably.

## Training for Visual Inspection of Single-Use Technologies (SUTs)

One of the instructional videos produced by Pall and Lonza addresses best practices for visual assessment of SUTs. Operators must understand how to inspect disposables effectively without damaging them. This video highlights different cosmetic and potentially dangerous defects that can be found on several SUT types. It also instructs operators on how to handle such technologies appropriately during visual inspections. By following the steps outlined in the video, operators can be assured that they will perform inspections safely and effectively in alignment with industry recommendations, such as those provided by the BioPhorum Supply Reliability Base (**4**).

These instructional videos can help end users to ensure current good manufacturing practice compliance by providing **STANDARDIZED**, **ON-DEMAND** training that can be implemented within or across companies as needed — and learners can work at their own pace.

Trainers also must consider that access to operational single-use systems and cleanroom suites will be limited in commercial environments.

Lonza and Pall's program started with face-to-face instruction supported by videos and practical exams. Over time, emphasis was placed on developing self-directed programs for all levels of learning and understanding. Those were offered as on-demand digital solutions, with delivery formats spanning from traditional digital media to VR using HoloLens devices (Microsoft). In essence, training must support transfer of knowledge, skills, and attitudes required for consistently strong performance.

### First Projects: From Simple to Complex

Initial trainings focused on demonstrating use of a simple technology (Pall's Kleenpak sterile connectors) before progressing to instruction about complex processes such as automated, single-use tangential-flow filtration (TFF). Course organizers discovered that much of the material designed for training of Pall employees on Pall products could be transferred easily to courses for end-user operators — in this case, at Lonza.

Organizers also learned that technical proficiency with SUT does not necessarily make someone a good trainer on SUT operation. Instructors must be strong facilitators and assessors as well as subject matter experts (SMEs). Pall, therefore, instituted a training program to help SMEs become competent trainers.

Lonza and Pall determined that training packages could be standardized easily by simplifying the training process and reducing the number of required materials. Furthermore, Lonza was able to leverage not only the operator training resources from Pall, but also the "train-the trainer" program, leading to a win–win situation for both companies.

### Joint Instructional Video Development

Lonza and Pall collaborated to develop instructional videos outlining best practices that are aligned with industry standards for working with several SUT types in different unit operations and for different biopharmaceutical modalities. For each video, the companies worked together to create a detailed storyboard based on training needs. The videos were filmed at Lonza in operational cleanrooms to provide good representations of biomanufacturing environments and thus to maximize potential knowledge transfer. Storyboard development and filming often yielded new ideas about communicating best practices for SUT handling and improving the training tools further.

Those efforts led to production of instructional videos that could be highly beneficial to the biopharmaceutical industry. Developed by Pall Corporation, these videos are accessible in the Accelerator e-Training Center, which presents a series of high-quality digital training tools for SUT use, handling, and operations (Figure 4).

As of December 2021, more than 200 short (<10 minutes), graphically enhanced instructional videos — "Mediabooks" — have been uploaded to the Accelerator e-Training Center. Those materials come without voiceovers and demonstrate equipment and process operations step by step. The content is available online at any time, with access provided in six languages (English, French, German, Spanish, Chinese, and Japanese).

The instructional videos can help end users to ensure CGMP compliance by providing standardized, on-demand training that can be implemented within or across companies as needed — and learners can work at their own pace. The Mediabook modules are designed for easy access, and they feature up-to-date

**Figure 4:** Example of digital training content to support handling of single-use technologies


content that emphasizes critical points in SUT implementation. Modules include highlights of important information and clear, detailed instruction about how — and how not — to work with each SUT and process. Process steps and interactive checklists can be downloaded and printed to minimize human errors during operation by ensuring that all steps are completed in the right order.

Within the Accelerator e-Training Center, learners can assess the skills that they have acquired using more than 40 "knowledge checks." Upon course completion, learners earn certificates that can serve as training records for CGMP qualification and as measures of training effectiveness and time to competence.

## The Importance of VR Training Tools

In 2020, the importance of virtual tools increased significantly. In fact, VR technology enabled Lonza to accelerate COVID-19 vaccine process development dramatically despite travel and personnel-interaction restrictions during the pandemic. Although VR training might seem to be frivolous and impractical, it is advanced and already has been implemented in many contexts. Medical students, aviators, and astronauts all train using VR. In the biopharmaceutical industry, Takeda Pharmaceuticals uses VR to train operators on aseptic practices (**6**).

Leveraging proven virtual- and augmented-reality technologies for muscle memory and real-time guidance in SUT training can decrease training time for new operators and increase training efficacy. By providing better, more engaging instruction, training effectiveness can be increased, helping to decrease human errors.

VR- and MR-based training decrease "door-to-floor" time by up to 50%, reduce training costs, eliminate trainer-time bottlenecks, increase new-hire productivity, and enable on-demand retraining without incurring additional expenses. Together, such benefits can help operators to perform at the levels that are required to make high-quality products — and to help prevent costly errors.

Even if VR cannot fully replace in-person training, it provides three main advantages (detailed below) that could significantly reduce time to competence, the number of requisite training resources, and human errors.

**Optimal Training Environments:** VR requires little setup time and few resources for trainers to repeat courses and provide refresher sessions. Meanwhile, learners can practice their lessons in safe environments before attending on-the-job training and be evaluated without requiring access to operational cleanrooms. VR also enables training under simulations of normal and abnormal conditions, facilitating instruction on proper responses to different problems.

**Immersible Experiences:** VR makes training feel real, helping to ingrain process sequences and improve eye–muscle coordination in ways that enable reliable execution of tasks. The "tactile" effect is especially important for SUT training. That can be simulated using commercially available tactile gloves.

## Features of Lonza's Virtual Reality (VR) Training Program

Lonza's VR training program for aseptic practices is designed to be accessible for operators with all levels of experience. Key system features include the following.

**Multiplayer software** enables users from across the world to meet, speak, and collaborate in real time as they interact with products in virtual environments.

**Recording tools** enable users to document and save events, meetings, interactive sessions, and product explanations. Thus, trainees and their companies can create, preserve, and share their own VR content.

**File-upload capabilities** ensure that presentations, images, videos, notes, and portable document files (PDFs) housed on a trainee's desktop can be shared with colleagues and business partners in the VR environment.

**Computer-aided design (CAD) compatibility** enables users to upload, view, share, and manipulate different CAD file formats with users across the globe in VR.

**Figure 5:** Examples of Lonza's virtual cleanroom training environment (IMAGES COURTESY OF LONZA AND REALWORLD ONE)


**Consistent Delivery:** VR-based training can provide integrated, immediate corrective feedback for pre-defined standard unit operations. It also can enable access to a virtual coach in tutorial mode.

## Starting with Aseptic Practices

Lonza initiated its program with tutorials on aseptic practices detailing how to move within a cleanroom and how to clean equipment properly. This module was a priority because its concepts apply to all CGMP production sites. In a virtual cleanroom, operators learned about movement speed, placement of objects, cleaning procedures, and so on, establishing muscle memory to improve consistency of performance. Such instruction can help decrease contamination risks in real work environments.

Lonza's digital transformation team worked with trainers and SMEs from Pall and other SUT suppliers to establish virtual suites with exact, fully interactable replicas of equipment to be used in production (Figure 5). Employees now can train at their own pace for 10 to 20 minutes at a time in these safe, virtual environments on how to handle and use the equipment — even before it is installed on the shop floor. Furthermore, learners can perform lessons and discuss topics in the same VR room with colleagues and trainers located at other Lonza sites around the world.

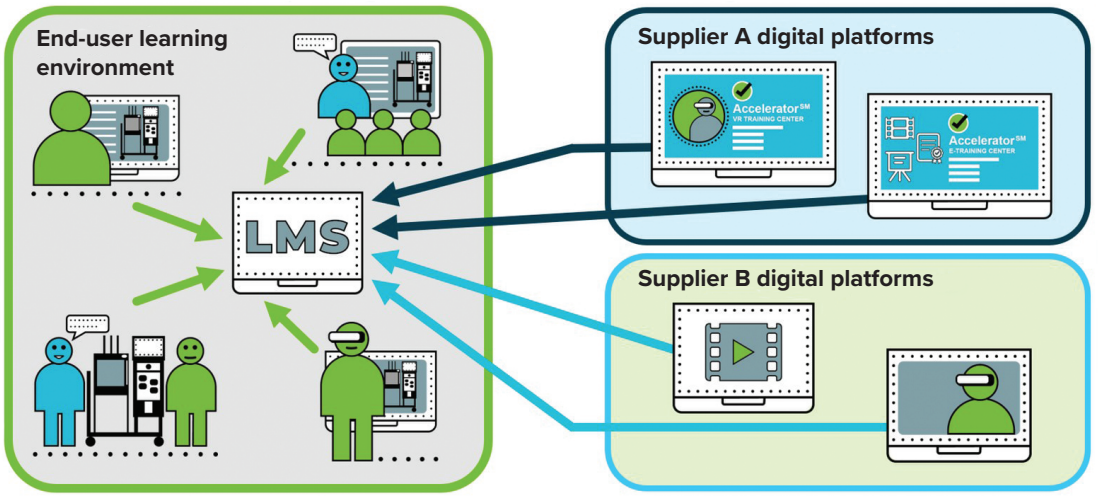
VR training is preceded by multiple short sessions (1–2 hours) in virtual classrooms. Those tutorials provide the technical training needed to establish a basic understanding of the equipment and processes that will be applied using VR/MR. Additional requirements such as videos, reading assignments, and written analyses together with the virtual classrooms ensure that all participants begin the VR/MR portion of the training with the same level of understanding.

The virtual cleanroom has been outfitted with simulated equipment such as pipettes and biosafety cabinets (BSCs), so users can experience sterile pipette assembly and cleaning and movement techniques realistically. Goals of the VR aseptic practices training program include a 25% reduction in operator errors as compared with those observed among traditionally trained employees and a 20% decrease in training time.

In the middle of 2020, select facilities piloted a beta version for specified standard unit operations in cleanrooms and BSCs. More sites will become involved pending the availability of VR hardware. New priorities include addition of other unit operations and standard equipment to the program and incorporation of VR technology enhancements (such as haptic gloves) for increased immersion in the content.

Lonza and Pall also collaborated on VR training for highly common SUT operations such as filter integrity testing and liquid/powder mixing. The development process highlighted the benefit of having a continuum of training assets from face-to-face instruction to high-quality video and ultimately

**Figure 6:** Interdependency of a virtual biopharmaceutical training ecosystem (LMS = learning management system)




VR training. The program also demonstrated the virtues of a truly blended training approach.

Based on those initial applications of VR training, Lonza intends to compare the effectiveness of digital and traditional training methods, quantifying their impacts on incidence of operator-related errors and validating their time of delivery.

Results from proof-of-concept testing at Lonza's biologics operations site in Visp, Switzerland, are promising. The studies show that millennials prefer VR to traditional delivery, with average user net promoter scores of 9.19 out of 10. VR modules also were more efficient, exhibiting a ~60% reduction in door-to-floor time. The technology's ability to reduce long-term incidence of human-caused errors still must be proven. The goals for a more comprehensive VR training program are to decrease the operator door-to-floor time by at least 50% and to increase quality by reducing human-triggered deviations by up to 80% due to more effective training and retraining.

## The Importance of Agility and Interconnectivity

Collaborative development of SUT training materials also uncovered the need for interconnectivity within and across training platforms. A learning management system (LMS) enables tracking of the multiple platforms needed to ensure that all employees are receiving the training that they need and in the formats that best suit their learning styles. An LMS also helps to capture all training records for GMP compliance within an organization.

The value of interconnectivity between SUT vendors and biopharmaceutical manufacturers on training development also has been demonstrated clearly. All parties involved in the drug development ecosystem must synergize the lessons and connections that come from training solutions, especially because significant interdependencies already exist among them.

## Collaboration Truly Works

Change is the primary constant in the biopharmaceutical industry. Teaching solutions must help employees to learn rapidly about new equipment and technologies as they are introduced. By sharing knowledge and relying on each other's expertise, Pall and Lonza have identified a combination of teaching methodologies that facilitates engaging and efficient training of SUT users of all skill levels. Cooperation shortened the timelines for training platform development and enhanced the quality of the resulting training tools.

The solutions that resulted from Lonza and Pall's collaboration represent a blended approach to SUT instruction, including both hands-on and digital learning as well as support from interactive simulation technologies. VR also represents a sustainable approach to training, one that integrates fully within industry 4.0 principles and the BioPhorum Digital Technologies Roadmap (**7**).

Most important, the training platforms developed by Pall and Lonza have been implemented and are benefiting both companies' employees. Work is ongoing to expand the number of Mediabook

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modules, interactive supporting documents, and knowledge checks in Pall's Accelerator e-Learning Platform. Program directors also are planning to add to the list of topics covered by Lonza's and Pall's respective VR platforms and to increase the number of Lonza sites with VR training capability.

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