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Opinion Article: Workforce Training for Pharmaceutical Manufacturing Operators

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Introduction

Training in the pharmaceutical industry is in dire need of a change. In my organization's cumulative decades of providing management, technical, and education consulting services to the pharmaceutical industry, we have rarely—if ever—encountered a client where training is seen as more than a series of procedural, bureaucratic, "check-the-box" activities. Training programs typically use some of the most outdated, least effective methods of teaching (1), and they are typically seen as an activity for compliance—not for education. Employees rarely understand what they're doing or why, and consequently, they make avoidable errors, and they're unable to recognize when processes are no longer in a state of control. Even in organizations that attempt to provide high-quality, meaningful training, a variety of obstacles often stand in the way, such as limited time from subject matter experts (SME's) or inability to access the proper training environments. However, new technologies offer the potential to revolutionize training in the pharmaceutical industry. We believe that virtual reality (VR) can bring pharmaceutical training into the 21st century, quickly and effectively educating large cohorts of employees who are not only competent at executing procedure, but who also understand the underlying fundamental principles behind their work.

The Poor State of Training in Pharma

To begin, it's helpful to review the current state of training in the pharmaceutical industry. Ineffective training programs are surprisingly similar and surprisingly universal. We see the same characteristics across the industry: from giant traditional generics multinationals to small, venture capital-backed cell-and-gene start-ups. At its heart, poor training is fundamentally transactional. Employees engage in activities that are generally acknowledged to have very little value but are performed simply for the sake of compliance-related accountability. The goal is typically to "check a box" that the activity has been completed, not to ensure that employees have learned and retained necessary knowledge. Of course, a key dilemma is that employees actually need real education: in the current market, many job roles are filled by individuals with no pharmaceutical background; even those hires with science-focused degrees are unlikely to have been introduced to the specifics of manufacturing or laboratory operations during their study.

A very common but highly ineffective training task is the oxymoronically named "Standard Operating Procedure (SOP) Read and Understand" activity. Employees are tasked with reading SOP documents, which may be dozens or hundreds of pages long. There is typically no assessment that indicates whether an employee actually understood or retained any of the information; employees may indicate that they have read the documents without ever doing so. Nonetheless, even if employees actually were to diligently read all of the assigned SOP's, the reading activity alone would not prepare employees to effectively complete a task. Not surprisingly, trainees often feel this type of activity is of little value (2).

After a trainee moves towards the conclusion of a particular training sequence, they will typically participate in "on the job training" (OJT), where they work with a more senior employee, often an SME.

On-the-job training may provide the most applicable learning that trainees experience, but it often has a limited focus on procedural execution. Trainees typically learn a rote set of actions, but it is rarer for them to be coached on the fundamentals behind what they are doing, why they are doing it, and the importance of their actions. Further, OJT tends to focus most heavily on how to perform actions in the correct manner: trainees don't always have the opportunity to understand the common mistakes and sources of error, or how to respond to "edge cases," such as when unusual or unplanned situations occur. Due to time and resource constraints, even training on the procedural aspects of work isn't always completed to mastery. Trainees may be coached to the point that they can successfully pass qualification activities, but they are often not fully comfortable and confident in their procedure.

An observer doesn't need a deep background in adult learning theory to recognize that the common training practices currently employed in the pharmaceutical industry are not particularly effective. While they may provide mediocre results at preparing employees to uncritically execute procedures, they are deeply deficient at preparing employees to function at a high cognitive level in their work, and within the management context of their organization.

The Challenges to Effective Training

Characteristics of ineffective training are common at most pharmaceutical organizations, and so too are the challenges to providing more effective and more meaningful training. Chief among these is that effective training requires significant time and resources. SME's typically have the knowledge to provide thorough and comprehensive instruction and coaching on specific procedures, while also connecting procedural work to fundamental background principles. However, SME's are typically overburdened, managing immediate operational issues, and they have very little time to devote to and develop meaningful training. It's also an uncomfortable truth that not every SME is a skilled trainer, and some of them struggle to patiently and effectively convey information to new learners. Even those SME's who excel at in-person instruction may not have the knowledge to develop a unified educational program that uses modern, innovative approaches of instructional design.

Physical resources can also represent a significant limitation. Critical areas and equipment are in use almost constantly and can't easily be taken out of service to accommodate training. Aseptic technique and behavior training and gowning practice may take place in regular office spaces. Trainees may not be able to work in equipment such as biosafety cabinets or isolators until final steps of qualification, and they instead practice work in simplistic wooden mock-ups. The high cost of consumables can also motivate less realistic training: we have heard anecdotes of plastic juice containers and cardboard shoe boxes serving as stand-ins for bioprocess bags and tube welders.

Employee turnover and rapid industry growth have also stretched training programs. Workers who are hired without prior background knowledge require additional attention to effectively train. There are currently reports of labor shortages (and their associated training challenges) across the pharmaceutical sector. However, there exists a "perfect storm" that is particularly acute in cell and gene therapy manufacturing. Growth in this area is occurring at a rapid pace, and experienced SME's are in short supply. Manufacturing personnel often perform a wide range of high-risk manual process steps, and their skill is critical to maintaining product quality. However, very few individuals currently possess these specialized skills, which are rarely taught in university degree programs. This unique situation requires

that organizations themselves deliver highly comprehensive training programs, but in an environment where time, facilities, and SME resources are more limited than in traditional manufacturing settings.

The Consequences of Ineffective Training

Concern with training isn't simply an academic exercise. Poor training has a tremendous negative impact. Our organization has helped many firms both large and small to manage, investigate, and remediate all manner of poor practices, deviations, failures, recalls, and other events. These are typically caused by a confluence of factors. But almost always, we find that poorly trained employees—who procedurally execute tasks without understanding what they're doing or why—play a critical, negative role. A recent study determined that 25% of quality defects in the industry can be attributed to human error, and it is the main source of product recalls (3).

There are hard costs associated with such events. By our industry analysis, a typical aseptic processing site experiences a range of these events annually with different frequencies, at an average cumulative cost of approximately $16 million: this ranges from deviations (that can cost between USD 10-20 thousand each) to recalls (upwards of USD 2.5 million or more). This estimation, of course, does not factor in the greater public health costs of drug supply disruptions, shortages, and price instability that can be caused by these events.

Costs are even greater in the cell and gene therapy space, where organizations may manufacture customized therapies using a patient's own cells. Seemingly small manufacturing errors can cause destruction of the product, and a patient can't simply be given a dose from another batch; they may die before another manufacturing cycle can be performed. The cost of a mistake is catastrophically high. In the cell and gene space in particular, inefficient training models themselves are decreasing the availability of therapies: because qualified personnel are in short supply, the slow speed and inefficiency with which new employees can be trained is increasingly viewed as a rate-limiting step in development and commercialization (4). These obstacles increase the cost of therapies, and risk making them unattainable to some patients and payors. Clearly, new modalities of workforce training are critically needed. We believe virtual reality (VR) can provide a revolutionary solution to many these training challenges.

A Brief Introduction to Virtual Reality

Before discussing the specific applications of virtual reality to training and to the pharmaceutical industry in general, we'll present a brief introduction to virtual reality as a medium. The term "virtual reality" is often used to refer to a variety of related but distinct technologies. For the purposes of this article, we'll define virtual reality as a technology that allows users to be fully immersed in a three-dimensional, simulated environment. Users can move within this virtual environment as if they were physically present in it. They can interact with virtual objects, by grasping items, using tools, and so forth. The technology can also monitor the user's actions to facilitate evaluation of user behaviors. Feedback may be provided in real-time or retrospectively.

These capabilities are enabled by specialized hardware. A head-mounted display (HMD) fits over the user's face like a large set of goggles, and it displays images on small screens directly in front of the eyes. The virtual environment is rendered stereoscopically such that it appears three-dimensional. The system tracks the user's head position and rotation, and it updates the images rendered to the screens in the HMD such that users can tilt, move or rotate their heads and have a full 360-degree view of the virtual environment just as they would in a physical environment. This near real-time rendering, along with audio and haptic feedback, provide the illusion of being physically present in the virtual world, a concept referred to as "presence." Hand and finger movements are also tracked (often by hand-held controllers), allowing the user to interact with virtual objects.

It's important to mention that not all technologies deemed "VR" allow this level of immersion. For example, videos that provide a 360-degree view are often referred to as "VR video." A viewer can watch the video in an HMD, turning their head to observe different parts of the scene, but since the video is pre-recorded, there is no opportunity for interaction. "VR tours" allow users to somewhat freely move through virtual environments, such as buildings or natural sites, but interaction with environmental elements is not possible. Both VR video and VR tours can also be consumed using an ordinary computer screen, which provides an even less immersive experience than an HMD.

In recent years, immersive virtual reality has experienced an explosion of attention and use in many areas. Although initial development began in the 1970's, it was not until the mid-2010's that affordable, reliable, and practical VR systems first appeared on the market. This has sparked the development of software programs, as well as interest in using VR for a wide variety of consumer and commercial applications. There is now a burgeoning ecosystem of diverse VR hardware and software, with some products focused on consumer entertainment purposes, and others used for more robust commercial and enterprise applications.

A Sidenote about Augmented Reality (AR)

One technology that is often confused and conflated with virtual reality is augmented reality, or AR. Although VR and AR are often mentioned together, they are very different. While the goal of VR is to place users in a virtual environment that is different from the space they are in, the goal of AR is to add visual or auditory information to what a user already sees in their physical environment. AR equipment often includes eyeglasses with transparent lenses that can overlay computer-generated images across the user's visual field. It usually also includes a computer vision system that can recognize and respond to objects in the user's environment. For example, in a theoretical industrial application, AR could provide instruction and visual guidance to an employee repairing a piece of equipment. A step-by-step repair procedure could appear in the user's view, and arrows appearing on top of various components could indicate how they should be adjusted. Although AR has significant potential to assist users in performing procedural tasks, we find it less robust as a fundamental training tool, because it cannot place users in simulated environments to practice and perfect new skills.

The Benefits of Virtual Reality as a Training Tool

VR is commonly associated with consumer entertainment, gaming, and social media, but the technology has rich roots in training and tremendous power as a tool for it. Much of the initial development of

immersive VR was funded by NASA to create training systems for astronauts, and it is now used for workforce development in many different industries.

VR can simulate real-life scenarios in a safe and controlled environment, allowing learners to gain practical experience without the risks, costs, and logistics associated with real-world training. Since systems can monitor body position and hand movements, users can learn and practice challenging physical manipulations to gain a "hands-on" level of understanding. Computerized coaching systems monitor the trainee's actions in real time, and they can immediately point out errors, demonstrate correct procedure, and provide opportunities for additional practice until trainees gain mastery. Additionally, VR is inclusive of different learning needs: it allows learners to practice and reach competency at their own pace.

While it is theoretically possible to create simulations that train workers on almost any physical task or procedure, some of the best uses of VR training involve high-risk situations or complex operations, such as those in emergency response, medicine, the armed forces, transportation, and construction. VR training also provides particular value for training in tasks that involve equipment or locations that are difficult or hazardous to access, or that cannot be easily replicated for training purposes. Examples include maintenance and operations involving wind turbines, offshore drilling platforms, or high-voltage transmission cables. Even for work that does not occur in exotic locations, VR removes constraints of resource availability and proximity.

Finally, VR can help to standardize training across different locations and time zones. With VR, employees can receive consistent training, regardless of their location, and they can access the training at any time, making it a convenient and flexible option. This can be particularly beneficial for multinational companies that need to train employees across different regions and sites, as it can reduce the need for expensive travel and accommodation costs associated with in-person training. A wide variety of studies, across many industries and use cases, have often found VR to be at least as efficacious as traditional training, and often more so (5).

The use cases for VR training in surgery may most closely parallel those in the pharmaceutical industry. Similar to laboratory analysts and manufacturing operators, surgeons must learn intricate, high-risk physical manipulations, and they must have the ability to practice repeatedly to ensure consistency. Learners must also connect background scientific information to manual practices; VR can assist in bridging this gap between theory and practice.

Virtual reality training in surgery shows very positive results. For example, one seminal study (6) examined virtual reality used to train surgical residents for performing laparoscopic cholecystectomy. The residents in the control group (trained using conventional methods) made on average three times as many errors and used 58% longer surgical time than those trained using virtual reality. VR training has been used for a wide variety of surgical procedures, and it has been studied extensively. Although the surgical studies are too voluminous to review in significant detail, meta-analyses have shown that VR-based training almost universally increases efficiency of training, decreases error rate, and increases procedure quality (7, 8, 9).

The Potential of Virtual Reality in the Pharmaceutical Industry

There are a number of ways that VR can specifically address some of the most pressing training challenges experienced in the pharmaceutical industry. For these situations, the strongest capabilities of VR center on instructional quality, scalability, resource independence, and pedagogical ability to link background theory to physical practice.

Compared to the training program elements typically found in pharmaceutical organizations, VR-based training is focused on the development and assessment of mastery, not on the mere completion of a particular training activity. Instead of simply reading a static SOP, learners can practice until they're comfortable and competent. However, learning benefits of VR extend beyond repetitive practice: learners can make mistakes, try again, and understand the consequences of incorrect actions. This increases the depth of knowledge about a procedure.

One of the most common obstacles to effective training in the pharmaceutical industry is the scarce availability of resources, whether they be facilities and equipment or the time of SME trainers. VR's ability to place users in immersive simulated environments removes this limitation. For example, learners can work with simulated and highly realistic BSC's, or they could practice their behavior in virtual cleanrooms. This is also a notable benefit for practicing certain activities that use high-cost consumables, such as those within the cell and gene sector.

Mentoring and coaching interaction can approximate some behaviors of an SME trainer. As learners perform and practice simulated activities in VR, software monitors behavior and provides coaching and feedback, in much the same way that an SME guides learners through hands-on activities. The feedback and coaching that VR systems provide are uniquely personalized to a trainee's actions and learning needs, and their progress can easily be summarized in assessment "score cards" that detail skills mastered and those that require more improvement.

In some respects, VR has particular benefits over human trainers. For example, VR provides consistent, unbiased, patient coaching and feedback in a way that human trainers cannot always do. Towards the end of a long day of supervising training activities, an SME may not be as vigilant or patient as they were at the beginning; VR is equally consistent no matter the situation. Since VR-based training is not limited by SME time and availability, if a trainee requires a long period of time to slowly improve their technique and achieve mastery, they can be easily accommodated. Additionally, VR software can monitor many variables at the same time: it can observe body position, speed of movement, and can also ensure that the steps of a procedure are being completed correctly. A human trainer may not be able to meaningfully focus on more than one of these variables simultaneously. Incidentally, we have observed that adult learners feel less self-conscious or embarrassed when making mistakes and receiving coaching in VR, as compared to when they work with a human trainer.

VR-based training solutions are also easily scalable in a way that SME-led sessions in the physical world are not. The number of learners that can be trained in VR at a particular time is limited only by the amount of VR equipment. Extra capacity can be created by simply acquiring additional sets of VR equipment, without needing to build more training suites or freeing up SME time.

It should be noted that, in our view, VR cannot fully replace the role of a human SME trainer. Instead, we see VR's role as an "SME extender." It can teach trainees much of the foundational information that

is covered in lengthy, repetitive training sessions that often do not use the SME's skills and knowledge to the fullest potential. Then, after acquisition of this knowledge, trainees can move onto more advanced, targeted sessions with SMEs, learning how to apply this information to product- and process-specific techniques, and preparing for OJT and task qualification activities.

Finally, VR can provide elements of hyper-realism that help trainees understand the background of why procedures must be completed in a certain way. For example, in a VR simulation, trainees can visualize (normally invisible) unidirectional airflow in a cleanroom environment, and they can explore how their movement disturbs it, creating turbulence and eddies. In such an experience, the rote learning directive of "slow and deliberate movement" is scaffolded and reinforced with a strong intuitive understanding of what happens when employees violate this practice. Trainees could also observe representations of where contamination might exist, and how potential contamination could slough off gowning if first air is violated during interventions. These types of activities can give learners a fundamental understanding of what they are doing and why, and they help to link theory and practice.

Time can also be manipulated within the simulated environment, giving trainees immediate understanding of the impact of their actions. For example, in a laboratory-based microbiology activity, bacterial colonies can grow on agar plates in seconds. This feature can immediately show a trainee whether their plate streaking technique correctly resulted in isolated colonies. In the real world, the specifics of how such a procedure was performed would typically be long forgotten by the time the results are available.

Adoption, Best Practices, and Study of Virtual Reality in the Pharmaceutical Industry

Despite tremendous potential, the pharmaceutical industry has only recently begun to implement VR-based training solutions. However, interest and activity in this area are rapidly growing. A small number of leading organizations provide off-the-shelf and customized VR training programs specifically for the pharmaceutical industry: these focus on manufacturing operations, laboratory procedure, or both. (Full disclosure: our own organization, Virtuosi, offers a variety of VR training products for different sectors of the pharmaceutical industry.) Some pharmaceutical organizations have retained contract development firms to create their own small VR training experiences in-house, but the details, extent, and efficacy of these programs is typically not widely reported externally. Finally, equipment manufacturers are increasingly creating VR training materials (often a mixture of 360-degree video and true immersive VR) to familiarize employees with operations on their specific equipment.

Just as with any other training tool, VR can also be misused, and it is not a panacea for every training challenge. Examples of poor implementation of VR abound, and negative experiences with these situations may hold back the industry's embrace of the technology. VR is fundamentally a physical medium, and it is best used to convey and monitor trainee actions and procedure completion. For example, rarely is it resource-effective to use VR to provide lecture-style content coverage. In fact, our own VR solutions are always paired with a video-based component that covers the fundamental background knowledge in a much more engaging manner than SOP reading or dry classroom PowerPoint presentations. After assimilating information from these videos, trainees are then ready to

enter the VR laboratory to learn and practice physical skills, and to understand how they connect to core principles.

Additionally, although VR can be customized to train an employee on an organization's highly specific equipment and procedures, such use cases run the risk of providing only transactional training. Unless such VR activities are very carefully designed, employees may simply be learning the procedure and nothing more: the deeper opportunities to understand what they are doing and why can be lost. VR is often best used to teach the fundamental, transferrable skills, such as how to move when performing interventions above a filling line, instead of how to perform interventions on a very specific filling line. VR training on generalized principles will ensure that employees understand the basics and can apply those principles in a variety of different situations. Additionally, companies that rely on VR that is highly specific to their operations will need to create a plan to update training software whenever procedures or equipment change; this is not a trivial concern.

Formal studies on VR in the pharmaceutical industry are limited but promising. A recent report (10) examined the implementation of a VR training activity at Novo Nordisk. The training activity focused on conducting and documenting a pH calibration and adjustment. One element of the study determined that theoretical knowledge gained from VR training was 39% higher than from reading the SOP and was equal to knowledge gained from SME-led training. Participants also found VR training to be highly enjoyable and engaging, when compared to SOP "read and understand" activities. Different elements of the study, as well as those conducted by other groups (11), suggest that VR may be most efficacious as a training tool when used in concert with certain elements of SME-led training. This mirrors our observations that VR provides an engaging and efficacious means of learning foundational content, but that SME trainers provide important value for taking trainees the "last kilometer."

Informal, anecdotal feedback from clients using our own product has also provided evidence of VR's effectiveness. Generally, clients report that trainees' time to competency is reduced by 30-50%, and error rates for those employees trained by VR are approximately 30% lower than those trained using conventional approaches. More specifically, a large CDMO using our product set up a comparison test between interns and experienced employees. Interns with a high school education learned serological pipetting and micropipetting techniques solely through video lectures and VR activities. After training was complete, the pipetting performance of the interns (assessed by measuring pipetting volume and technique error) matched that of experienced laboratory employees.

The Future of VR in Pharmaceutical Training

The pharmaceutical industry can be slow to change, but we hope that as more organizations incorporate VR into their training programs, they will experience and discuss the benefits, leading to a positive feedback cycle within the industry. Additionally, there are several possible near- and medium-term developments that may assist in the widespread adoption of Virtual Reality.

First, technology and equipment are advancing at a fast pace. VR systems continually become more powerful, less expensive, and more portable. Hand-tracking technologies are maturing quickly, and individual finger movements can be monitored with increasing precision, in some cases without the use of hand-held controllers. Eventually, glove-based controllers will provide full freedom of movement, and

they will also be able to provide accurate haptic feedback, giving users the tactile illusion of picking up and grasping various objects. For situations that involve significant movement, devices like multi-directional treadmills will allow users to freely walk through a simulation environment while remaining stationary in the physical world.

Currently, development of educational VR is a resource-intensive process, particularly when it is performed thoughtfully and in alignment with learning best practices. As the technology sees greater consumer and commercial use, it is likely that software tools (many of these likely driven by artificial intelligence) will emerge that automate certain aspects of the development process. Such advancements may also facilitate the creation of VR experiences customized for very specific situations, environments, and processes. However, in light of such a possibility, we reiterate our caution that overly customized VR training activities run the risk of becoming rote and transactional.

At a higher, programmatic level, as VR implementations become more common throughout the pharmaceutical industry, different projects and organizations will use different approaches; collectively, the industry will benefit from observing varied outcomes and determining best practices.

Finally, we hope that the recent increase of interest in the evaluation and modification of training practices will facilitate and encourage the implementation of VR. It appears that the industry is gradually developing a collective sense that continuing to train “the old way” will not effectively address current and upcoming challenges. We believe that VR can be an invaluable component of a new paradigm of training. It will benefit employees, organizations, and—most importantly—the patients we serve.

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