

Single-Use Process Equipment for Biopharmaceutical Manufacturing

As more and more companies are finding the value in outsourcing the manufacturing of their biopharmaceutical products to Contract Manufacturing Organizations (CMOs), the CMOs are, in turn, seeking new ways to increase productivity, product quality, and process efficiency. One of the technologies being rapidly adopted in the biopharmaceutical manufacturing industry is single-use, or disposable, process equipment and systems. Because CMOs are committed to providing the highest quality service possible to their clients, this often means making significant changes to stay up-to-date with the latest advances in manufacturing technology.

Disposable process equipment has actually been in use in various forms since the 1970's. However, at its inception, the available items were primarily limited to membrane filters and blood bags. Fast forward 40 years to today's manufacturing facilities and one can find an incredibly diverse array of single-use equipment and systems capable of handling almost any challenge associated with biopharmaceutical manufacturing. For operation in multiproduct facilities, disposable equipment provides increased flexibility with regard to raw materials and cell systems and can lead to faster turnaround times.

Converting an Existing Facility

Sooner or later, CMOs will likely begin to discuss whether or not to convert their existing processes and equipment to accommodate the use of disposables. Depending on the scope and scale of the manufacturing activities, this can seem like an enormous undertaking. This process is much like a Technology Transfer and CMOs should allow sufficient time to source materials and complete the engineering phase to determine the design and flow of the facility. Finally, integration and qualification of the new equipment must be completed prior to resuming manufacturing activities.

Because the cost for each new piece of single-use equipment can be much higher for larger systems, it is typically best suited for CMOs who produce smaller batches of multiple products. It is also essential to note that a facility does not have to operate solely on disposable equipment to experience the advantages that they can offer. Many facilities operate in a "hybrid" environment in which some processes are still run in stainless steel equipment (i.e. a large bioreactor for bacterial fermentation), while others, like chromatography for purification, can be completed in a system composed entirely of single-use apparatuses.

The use of disposables in day-to-day manufacturing operations can greatly reduce capital expenditures over the long run, but upfront costs may appear high to some smaller companies. Fortunately for CMOs, the disposable manufacturing industry has become quite competitive in recent years, allowing CMOs the luxury of price comparison between brands and the benefit of learning from other companies who have made the switch before them.

Cleaning Validation and Cross-Contamination

While cost effectiveness may be one of the determining factors in deciding whether or not to switch to disposables, the impact this technology can have on the product itself is the most critical. In all multiproduct manufacturing facilities, cross-contamination is a serious concern and one that CMOs, especially those operating under cGMP, cannot afford to lose sight of. Cleaning is necessary to remove product and non-product materials which could contaminate systems, effect product health and/or the quality of the therapy being provided.

Disposable technology has the benefit of reducing the opportunities for cross-contamination between products. New, pre-sterilized equipment is used for each new product and disposed of as biohazard waste upon completion of manufacturing activities. This removes the need for cleaning validation for each piece of equipment used. The result is not only a shorter manufacturing time, but also a reduction in costs related to labor that would otherwise be needed to clean, sanitize, and verify sterility and cleanliness of each piece of equipment before and after each manufacturing project.

It is also important to realize that cleaning validation involves more than just the Manufacturing Technicians operating the equipment. Both Quality Control and Quality Assurance are involved in the review and validation of testing and documents as they pertain to cleaning. Disposable equipment can have a major impact on price per project for clients and on the amount of time a project takes from start to finish based on this factor alone.

How VGXI Uses Disposable Equipment

The appeal of DNA Vaccines is due in large part to the ability of DNA to remain stable in an unrefrigerated environment longer than other biologic materials (i.e. viruses and proteins). However, because plasmid DNA is so stable, it requires a large investment in labor and a multistep process to fully remove it from equipment following manufacturing activities. For this reason, among others, VGXI has converted both their Process Development laboratory and cGMP production facility for the use of single-use systems.

While VGXI still utilizes stainless steel bioreactors for *E. coli* fermentations, processes such as cell lysis, purification, and fill/finish have all been adapted to use disposable equipment. Purification, for example, consists of chromatography to remove unwanted contaminants such as host-cell RNA and genomic DNA, endotoxins, and other cellular debris. Through the utilization of disposable columns, membranes and cassettes, VGXI has achieved up to 20x the binding capacity of conventional resins, has increased process throughput and compliance by no longer requiring cleaning validation, and has entirely eliminated the use of organics, carcinogens, flammables, and animal-based products.

Progressing Technology

Even though single-use systems have come a long way since the 1970s, the technology is still evolving. Again, for many companies, the initial investment in disposables may be too large to overcome. However, as further advancements are made and new materials and products become available, it may make more sense for existing facilities to make the change in the future. Additionally, because not all equipment is cost effective for day-to-day manufacturing activities at this time, facilities like VGXI who currently only take advantage of disposables in critical steps may make the switch to an entirely disposable system when the cost of investment can be outweighed by the long-term savings.

Whenever possible, CMOs should take every action available to increase process throughput, cost efficiency, and product quality for their clients. Unlike bell bottom jeans and blouses with shoulder pads, disposable technology is one trend that will not be going out of style anytime soon. In fact, it is likely to become an industry standard as new technologies are developed with disposable equipment as their foundation.

For more information on how VGXI implemented and uses single-use systems, please feel free to contact us by phone or email at (281) 296-7300 or info@vgxii.com.

About VGXI

VGXI is a contract manufacturing organization that specializes in the production of DNA plasmids under GMP for human clinical trials. With over 13 years' experience, we have produced products for numerous clinical trials in the U.S., Europe, Asia, and Australia. Our patented AIRMIX® manufacturing technology produces the highest quality plasmids in the industry with plasmid supercoil percentages up to 99% and final product concentrations as high as 15 mg/ml. Our highly experienced team can work with your project's unique requirements to create a manufacturing solution that ensures the success of your clinical program.

